

DESCRIPTION**OLIGONUCLEOTIDE MEDIATED INHIBITION OF HEPATITIS B VIRUS AND
HEPATITIS C VIRUS REPLICATION**

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Background Of The Invention

This patent application is a continuation of International Application No. PCT/US02/09187, with international filing date of March 26, 2002, published in English under PCT Article 21(2), which claims the benefit of Macejak et al., USSN (60/296,876),
10 filed June 8, 2001, Macejak et al., USSN (60/335,059), filed October 24, 2001, Morrissey et al., USSN (60/337,055), filed December 5, 2001, Beigelman et al., USSN (60/358,580), filed February 20, 2002, Beigelman et al., USSN (60/363,124), filed March 11, 2002, and which is a continuation-in-part of Blatt et al., USSN (09/817,879), filed March 26, 2001, which is a continuation-in-part of Blatt et al., USSN (09/740,332), filed December 18, 2000, which is a
15 continuation-in-part of Blatt et al., USSN (09/611,931), filed July 7, 2000, which is a continuation-in-part of Blatt et al., USSN (09/504,321), filed February 15, 2000, which is a continuation-in-part of Blatt et al., USSN (09/274,553), filed March 23, 1999, which is a continuation-in-part of Blatt et al., USSN (09/257,608), filed February 24, 1999 (abandoned), which claims the benefit of Blatt et al., USSN (60/100,842), filed September 18, 1998, and
20 McSwiggen et al., USSN (60/083,217) filed April 27, 1998. This patent application is also a continuation-in-part of Draper et al., USSN (09/877,478) filed June 8, 2001, which is a continuation-in-part of Draper et al., USSN (09/696,347), filed October 24, 2000, which is a continuation-in-part of Draper et al., USSN (09/636,385), filed August 9, 2000, which is a continuation-in-part of Draper et al., USSN (09/531,025), filed March 20, 2000, which is a
25 continuation-in-part of Draper et al., USSN (09/436,430), filed November 8, 1999, which is a continuation of Draper et al., USSN (08/193,627), filed February 7, 1994, now US patent No. 6,017,756, which is a continuation of Draper et al., USSN (07/882,712), filed May 14, 1992, now abandoned. All of these listed applications are hereby incorporated by reference herein in their entireties, including the drawings.

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The present invention concerns compounds, compositions, and methods for the study, diagnosis, and treatment of degenerative and disease states related to hepatitis B virus (HBV) and hepatitis C virus (HCV) infection, replication and gene expression. Specifically, the invention relates to nucleic acid molecules used to modulate expression of HBV and HCV. In addition, the instant invention relates to methods, models and systems for screening inhibitors of HBV and HCV replication and propagation.

The following is a discussion of relevant art pertaining to hepatitis B virus (HBV) and hepatitis C virus (HCV). The discussion is not meant to be complete and is provided only for understanding of the invention that follows. The summary is not an admission that any of the work described below is prior art to the claimed invention.

In 1989, the Hepatitis C Virus (HCV) was determined to be an RNA virus and was identified as the causative agent of most non-A non-B viral Hepatitis (Choo *et al.*, *Science*. 1989; 244:359-362). Unlike retroviruses such as HIV, HCV does not go through a DNA replication phase and no integrated forms of the viral genome into the host chromosome have been detected (Houghton *et al.*, *Hepatology* 1991;14:381-388). Rather, replication of the coding (plus) strand is mediated by the production of a replicative (minus) strand leading to the generation of several copies of plus strand HCV RNA. The genome consists of a single, large, open-reading frame that is translated into a polyprotein (Kato *et al.*, *FEBS Letters*. 1991; 280: 325-328). This polyprotein subsequently undergoes post-translational cleavage, producing several viral proteins (Leinbach *et al.*, *Virology*. 1994: 204:163-169).

Examination of the 9.5-kilobase genome of HCV has demonstrated that the viral nucleic acid can mutate at a high rate (Smith *et al.*, *Mol. Evol.* 1997 45:238-246). This rate of mutation has led to the evolution of several distinct genotypes of HCV that share approximately 70% sequence identity (Simmonds *et al.*, *J. Gen. Virol.* 1994;75 :1053-1061). It is important to note that these sequences are evolutionarily quite distant. For example, the genetic identity between humans and primates such as the chimpanzee is approximately 98%. In addition, it has been demonstrated that an HCV infection in an individual patient is composed of several distinct and evolving quasispecies that have 98% identity at the RNA level. Thus, the HCV genome is hypervariable and continuously changing. Although the HCV genome is hypervariable, there are 3 regions of the genome that are highly conserved. These conserved sequences occur in the 5' and 3' non-coding regions as well as the 5'-end of the core protein coding region and are thought to be vital for HCV RNA replication as well as translation of the HCV polyprotein. Thus, therapeutic agents that target these conserved HCV genomic regions can have a significant impact over a wide range of HCV genotypes. Moreover, it is unlikely that drug resistance will occur with enzymatic nucleic acids specific to conserved regions of the HCV genome. In contrast, therapeutic modalities that target

inhibition of enzymes such as the viral proteases or helicase are likely to result in the selection for drug resistant strains since the RNA for these viral encoded enzymes is located in the hypervariable portion of the HCV genome.

After initial exposure to HCV, the patient experiences a transient rise in liver enzymes, which indicates the occurrence of inflammatory processes (Alter *et al.*, IN: Seeff LB, Lewis JH, eds. *Current Perspectives in Hepatology*. New York: Plenum Medical Book Co; 1989:83-89). This elevation in liver enzymes will occur at least 4 weeks after the initial exposure and can last for up to two months (Farci *et al.*, *New England Journal of Medicine*. 1991;325:98-104). Prior to the rise in liver enzymes, it is possible to detect HCV RNA in the patient's serum using RT-PCR analysis (Takahashi *et al.*, *American Journal of Gastroenterology*. 1993;88:2:240-243). This stage of the disease is called the acute stage and usually goes undetected since 75% of patients with acute viral hepatitis from HCV infection are asymptomatic. The remaining 25% of these patients develop jaundice or other symptoms of hepatitis.

Acute HCV infection is a benign disease, however, and as many as 80% of acute HCV patients progress to chronic liver disease as evidenced by persistent elevation of serum alanine aminotransferase (ALT) levels and by continual presence of circulating HCV RNA (Sherlock, *Lancet* 1992; 339:802). The natural progression of chronic HCV infection over a 10 to 20 year period leads to cirrhosis in 20 to 50% of patients (Davis *et al.*, *Infectious Agents and Disease* 1993;2:150:154) and progression of HCV infection to hepatocellular carcinoma has been well documented (Liang *et al.*, *Hepatology*. 1993; 18:1326-1333; Tong *et al.*, *Western Journal of Medicine*, 1994; Vol. 160, No. 2: 133-138). There have been no studies that have determined sub-populations that are most likely to progress to cirrhosis and/or hepatocellular carcinoma, thus all patients have equal risk of progression.

It is important to note that the survival for patients diagnosed with hepatocellular carcinoma is only 0.9 to 12.8 months from initial diagnosis (Takahashi *et al.*, *American Journal of Gastroenterology*. 1993;88:2:240-243). Treatment of hepatocellular carcinoma with chemotherapeutic agents has not proven effective and only 10% of patients will benefit from surgery due to extensive tumor invasion of the liver (Trinchet *et al.*, *Presse Medicin*. 1994;23:831-833). Given the aggressive nature of primary hepatocellular carcinoma, the only viable treatment alternative to surgery is liver transplantation (Pichlmayr *et al.*, *Hepatology*. 1994;20:33S-40S).

Upon progression to cirrhosis, patients with chronic HCV infection present with clinical features, which are common to clinical cirrhosis regardless of the initial cause (D'Amico *et al.*, *Digestive Diseases and Sciences*. 1986;31:5: 468-475). These clinical features can include: bleeding esophageal varices, ascites, jaundice, and encephalopathy (Zakim D, Boyer TD. *Hepatology a textbook of liver disease*. Second Edition Volume 1.

1990 W.B. Saunders Company. Philadelphia). In the early stages of cirrhosis, patients are classified as compensated, meaning that although liver tissue damage has occurred, the patient's liver is still able to detoxify metabolites in the blood-stream. In addition, most patients with compensated liver disease are asymptomatic and the minority with symptoms report only minor symptoms such as dyspepsia and weakness. In the later stages of cirrhosis, patients are classified as decompensated meaning that their ability to detoxify metabolites in the bloodstream is diminished and it is at this stage that the clinical features described above will present.

In 1986, D'Amico *et al.* described the clinical manifestations and survival rates in 1155 patients with both alcoholic and viral associated cirrhosis (D'Amico *supra*). Of the 1155 patients, 435 (37%) had compensated disease although 70% were asymptomatic at the beginning of the study. The remaining 720 patients (63%) had decompensated liver disease with 78% presenting with a history of ascites, 31% with jaundice, 17% had bleeding and 16% had encephalopathy. Hepatocellular carcinoma was observed in six (.5%) patients with compensated disease and in 30 (2.6%) patients with decompensated disease.

Over the course of six years, the patients with compensated cirrhosis developed clinical features of decompensated disease at a rate of 10% per year. In most cases, ascites was the first presentation of decompensation. In addition, hepatocellular carcinoma developed in 59 patients who initially presented with compensated disease by the end of the six-year study.

With respect to survival, the D'Amico study indicated that the five-year survival rate for all patients on the study was only 40%. The six-year survival rate for the patients who initially had compensated cirrhosis was 54%, while the six-year survival rate for patients who initially presented with decompensated disease was only 21%. There were no significant differences in the survival rates between the patients who had alcoholic cirrhosis and the patients with viral related cirrhosis. The major causes of death for the patients in the D'Amico study were liver failure in 49%; hepatocellular carcinoma in 22%; and, bleeding in 13% (D'Amico *supra*).

Chronic Hepatitis C is a slowly progressing inflammatory disease of the liver, mediated by a virus (HCV) that can lead to cirrhosis, liver failure and/or hepatocellular carcinoma over a period of 10 to 20 years. In the US, it is estimated that infection with HCV accounts for 50,000 new cases of acute hepatitis in the United States each year (NIH Consensus Development Conference Statement on Management of Hepatitis C March 1997). The prevalence of HCV in the United States is estimated at 1.8% and the CDC places the number of chronically infected Americans at approximately 4.5 million people. The CDC also estimates that up to 10,000 deaths per year are caused by chronic HCV infection. The prevalence of HCV in the United States is estimated at 1.8% and the CDC places the number

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Numerous well controlled clinical trials using interferon (IFN-alpha) in the treatment of chronic HCV infection have demonstrated that treatment three times a week results in lowering of serum ALT values in approximately 50% (range 40% to 70%) of patients by the end of 6 months of therapy (Davis *et al.*, *New England Journal of Medicine* 1989; 321:1501-1506; Marcellin *et al.*, *Hepatology*. 1991; 13:393-397; Tong *et al.*, *Hepatology* 1997;26:747-754; Tong *et al.*, *Hepatology* 1997 26(6): 1640-1645). However, following cessation of interferon treatment, approximately 50% of the responding patients relapsed, resulting in a "durable" response rate as assessed by normalization of serum ALT concentrations of approximately 20 to 25%.

In recent years, direct measurement of the HCV RNA has become possible through use of either the branched-DNA or Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) analysis. In general, the RT-PCR methodology is more sensitive and leads to more accurate assessment of the clinical course (Tong *et al.*, *supra*). Studies that have examined six months of type 1 interferon therapy using changes in HCV RNA values as a clinical endpoint have demonstrated that up to 35% of patients will have a loss of HCV RNA by the end of therapy (Marcellin *et al.*, *supra*). However, as with the ALT endpoint, about 50% of the patients relapse six months following cessation of therapy resulting in a durable virologic response of only 12% (Marcellin *et al.*, *supra*). Studies that have examined 48 weeks of therapy have demonstrated that the sustained virological response is up to 25% (NIH consensus statement: 1997). Thus, standard of care for treatment of chronic HCV infection with type 1 interferon is now 48 weeks of therapy using changes in HCV RNA concentrations as the primary assessment of efficacy (Hoofnagle *et al.*, *New England Journal of Medicine* 1997; 336(5) 347-356).

Side effects resulting from treatment with type 1 interferons can be divided into four general categories, which include 1. Influenza-like symptoms; 2. Neuropsychiatric; 3. Laboratory abnormalities; and, 4. Miscellaneous (Dushieko *et al.*, *Journal of Viral Hepatitis*. 1994:1:3-5). Examples of influenza-like symptoms include; fatigue, fever; myalgia; malaise; appetite loss; tachycardia; rigors; headache and arthralgias. The influenza-like symptoms are usually short-lived and tend to abate after the first four weeks of dosing (Dushieko *et al.*, *supra*). Neuropsychiatric side effects include: irritability, apathy; mood changes; insomnia; cognitive changes and depression. The most important of these neuropsychiatric side effects is depression and patients who have a history of depression should not be given type 1 interferon. Laboratory abnormalities include; reduction in myeloid cells including granulocytes, platelets and to a lesser extent red blood cells. These changes in blood cell counts rarely lead to any significant clinical sequelae (Dushieko *et al.*, *supra*). In addition,

increases in triglyceride concentrations and elevations in serum alanine and aspartate aminotransferase concentration have been observed. Finally, thyroid abnormalities have been reported. These thyroid abnormalities are usually reversible after cessation of interferon therapy and can be controlled with appropriate medication while on therapy. Miscellaneous
 5 side effects include nausea; diarrhea; abdominal and back pain; pruritus; alopecia; and rhinorrhea. In general, most side effects will abate after 4 to 8 weeks of therapy (Dushieko *et al.*, *supra*).

Type 1 Interferon is a key constituent of many treatment programs for chronic HCV infection. Treatment with type 1 interferon induces a number of genes and results in an
 10 antiviral state within the cell. One of the genes induced is 2', 5' oligoadenylate synthetase, an enzyme that synthesizes short 2', 5' oligoadenylate (2-5A) molecules. Nascent 2-5A subsequently activates a latent RNase, RNase L, which in turn nonspecifically degrades viral RNA.

Chronic hepatitis B is caused by an enveloped virus, commonly known as the hepatitis
 15 B virus or HBV. HBV is transmitted via infected blood or other body fluids, especially saliva and semen, during delivery, sexual activity, or sharing of needles contaminated by infected blood. Individuals may be "carriers" and transmit the infection to others without ever having experienced symptoms of the disease. Persons at highest risk are those with multiple sex partners, those with a history of sexually transmitted diseases, parenteral drug users, infants
 20 born to infected mothers, "close" contacts or sexual partners of infected persons, and healthcare personnel or other service employees who have contact with blood. Transmission is also possible via tattooing, ear or body piercing, and acupuncture; the virus is also stable on razors, toothbrushes, baby bottles, eating utensils, and some hospital equipment such as respirators, scopes and instruments. There is no evidence that HBsAg positive food handlers
 25 pose a health risk in an occupational setting, nor should they be excluded from work. Hepatitis B has never been documented as being a food-borne disease. The average incubation period is 60 to 90 days, with a range of 45 to 180; the number of days appears to be related to the amount of virus to which the person was exposed. However, determining the length of incubation is difficult, since onset of symptoms is insidious. Approximately
 30 50% of patients develop symptoms of acute hepatitis that last from 1 to 4 weeks. Two percent or less of these individuals develop fulminant hepatitis resulting in liver failure and death.

The determinants of severity include: (1) The size of the dose to which the person was exposed; (2) the person's age with younger patients experiencing a milder form of the
 35 disease; (3) the status of the immune system with those who are immunosuppressed experiencing milder cases; and (4) the presence or absence of co-infection with the Delta

virus (hepatitis D), with more severe cases resulting from co-infection. In symptomatic cases, clinical signs include loss of appetite, nausea, vomiting, abdominal pain in the right upper quadrant, arthralgia, and tiredness/loss of energy. Jaundice is not experienced in all cases, however, jaundice is more likely to occur if the infection is due to transfusion or percutaneous serum transfer, and it is accompanied by mild pruritus in some patients. Bilirubin elevations are demonstrated in dark urine and clay-colored stools, and liver enlargement may occur accompanied by right upper-quadrant pain. The acute phase of the disease may be accompanied by severe depression, meningitis, Guillain-Barré syndrome, myelitis, encephalitis, agranulocytosis, and/or thrombocytopenia.

Hepatitis B is generally self-limiting and will resolve in approximately 6 months. Asymptomatic cases can be detected by serologic testing, since the presence of the virus leads to production of large amounts of HBsAg in the blood. This antigen is the first and most useful diagnostic marker for active infections. However, if HBsAg remains positive for 20 weeks or longer, the person is likely to remain positive indefinitely and is now a carrier. While only 10% of persons over age 6 who contract HBV become carriers, 90% of infants infected during the first year of life do so.

Hepatitis B virus (HBV) infects over 300 million people worldwide (Imperial, 1999, *Gastroenterol. Hepatol.*, 14 (suppl), S1-5). In the United States, approximately 1.25 million individuals are chronic carriers of HBV as evidenced by the fact that they have measurable hepatitis B virus surface antigen HBsAg in their blood. The risk of becoming a chronic HBsAg carrier is dependent upon the mode of acquisition of infection as well as the age of the individual at the time of infection. For those individuals with high levels of viral replication, chronic active hepatitis with progression to cirrhosis, liver failure and hepatocellular carcinoma (HCC) is common, and liver transplantation is the only treatment option for patients with end-stage liver disease from HBV.

The natural progression of chronic HBV infection over a 10 to 20 year period leads to cirrhosis in 20-to-50% of patients and progression of HBV infection to hepatocellular carcinoma has been well documented. There have been no studies that have determined sub-populations that are most likely to progress to cirrhosis and/or hepatocellular carcinoma, thus all patients have equal risk of progression.

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viable treatment alternative to surgery is liver transplantation (Pichlmayr *et al.*, 1994, *Hepatology.*, 20, 33S-40S).

Upon progression to cirrhosis, patients with chronic HCV and HBV infection present with clinical features, which are common to clinical cirrhosis regardless of the initial cause (D'Amico *et al.*, 1986, *Digestive Diseases and Sciences*, 31, 468-475). These clinical features may include: bleeding esophageal varices, ascites, jaundice, and encephalopathy (Zakim D, Boyer TD. *Hepatology a textbook of liver disease*, Second Edition Volume 1. 1990 W.B. Saunders Company. Philadelphia). In the early stages of cirrhosis, patients are classified as compensated, meaning that although liver tissue damage has occurred, the patient's liver is still able to detoxify metabolites in the blood-stream. In addition, most patients with compensated liver disease are asymptomatic and the minority with symptoms report only minor symptoms such as dyspepsia and weakness. In the later stages of cirrhosis, patients are classified as decompensated meaning that their ability to detoxify metabolites in the bloodstream is diminished and it is at this stage that the clinical features described above will present.

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Hepatitis B virus is a double-stranded circular DNA virus. It is a member of the Hepadnaviridae family. The virus consists of a central core that contains a core antigen (HBcAg) surrounded by an envelope containing a surface protein/surface antigen (HBsAg) and is 42 nm in diameter. It also contains an e antigen (HBeAg), which, along with HBcAg and HBsAg, is helpful in identifying this disease.

In HBV virions, the genome is found in an incomplete double-stranded form. HBV uses a reverse transcriptase to transcribe a positive-sense full length RNA version of its genome back into DNA. This reverse transcriptase also contains DNA polymerase activity and thus begins replicating the newly synthesized minus-sense DNA strand. However, it appears that the core protein encapsidates the reverse-transcriptase/polymerase before it completes replication.

From the free-floating form, the virus must first attach itself specifically to a host cell membrane. Viral attachment is one of the crucial steps that determines host and tissue specificity. However, currently there are no *in vitro* cell-lines that can be infected by HBV. There are some cells lines, such as HepG2, which can support viral replication only upon transient or stable transfection using HBV DNA.

After attachment, fusion of the viral envelope and host membrane must occur to allow the viral core proteins containing the genome and polymerase to enter the cell. Once inside, the genome is translocated to the nucleus where it is repaired and cyclized.

The complete closed circular DNA genome of HBV remains in the nucleus and gives rise to four transcripts. These transcripts initiate at unique sites but share the same 3'-ends. The 3.5-kb pregenomic RNA serves as a template for reverse transcription and also encodes the nucleocapsid protein and polymerase. A subclass of this transcript with a 5'-end extension codes for the precore protein that, after processing, is secreted as HBV e antigen. The 2.4-kb RNA encompasses the pre-S1 open reading frame (ORF) that encodes the large surface protein. The 2.1-kb RNA encompasses the pre-S2 and S ORFs that encode the middle and small surface proteins, respectively. The smallest transcript (~0.8-kb) codes for the X protein, a transcriptional activator.

Multiplication of the HBV genome begins within the nucleus of an infected cell. RNA polymerase II transcribes the circular HBV DNA into greater-than-full length mRNA. Since the mRNA is longer than the actual complete circular DNA, redundant ends are formed. Once produced, the pregenomic RNA exits the nucleus and enters the cytoplasm.

The packaging of pregenomic RNA into core particles is triggered by the binding of the HBV polymerase to the 5' epsilon stem-loop. RNA encapsidation is believed to occur as

soon as binding occurs. The HBV polymerase also appears to require associated core protein in order to function. The HBV polymerase initiates reverse transcription from the 5' epsilon stem-loop three to four base pairs at which point the polymerase and attached nascent DNA are transferred to the 3' copy of the DR1 region. Once there, the (-)DNA is extended by the HBV polymerase while the RNA template is degraded by the HBV polymerase RNase H activity. When the HBV polymerase reaches the 5' end, a small stretch of RNA is left undigested by the RNase H activity. This segment of RNA is comprised of a small sequence just upstream and including the DR1 region. The RNA oligomer is then translocated and annealed to the DR2 region at the 5' end of the (-)DNA. It is used as a primer for the (+)DNA synthesis which is also generated by the HBV polymerase. It appears that the reverse transcription as well as plus strand synthesis may occur in the completed core particle.

Since the pregenomic RNA is required as a template for DNA synthesis, this RNA is an excellent target for nucleic acid based therapeutics. Nucleoside analogues that have been documented to modulate HBV replication target the reverse transcriptase activity needed to convert the pregenomic RNA into DNA. Nucleic acid decoy and aptamer modulation of HBV reverse transcriptase would be expected to result in a similar modulation of HBV replication.

Current therapeutic goals of treatment are three-fold: to eliminate infectivity and transmission of HBV to others, to arrest the progression of liver disease and improve the clinical prognosis, and to prevent the development of hepatocellular carcinoma (HCC).

Interferon alpha use is the most common therapy for HBV; however, recently Lamivudine (3TC®) has been approved by the FDA. Interferon alpha (IFN-alpha) is one treatment for chronic hepatitis B. The standard duration of IFN-alpha therapy is 16 weeks, however, the optimal treatment length is still poorly defined. A complete response (HBV DNA negative HBeAg negative) occurs in approximately 25% of patients. Several factors have been identified that predict a favorable response to therapy including: High ALT, low HBV DNA, being female, and heterosexual orientation.

There is also a risk of reactivation of the hepatitis B virus even after a successful response, this occurs in around 5% of responders and normally occurs within 1 year.

Side effects resulting from treatment with type 1 interferons can be divided into four general categories including: Influenza-like symptoms, neuropsychiatric, laboratory abnormalities, and other miscellaneous side effects. Examples of influenza-like symptoms include, fatigue, fever, myalgia, malaise, appetite loss, tachycardia, rigors, headache and

arthralgias. The influenza-like symptoms are usually short-lived and tend to abate after the first four weeks of dosing (Dusheiko *et al.*, 1994, *Journal of Viral Hepatitis*, 1, 3-5). Neuropsychiatric side effects include irritability, apathy, mood changes, insomnia, cognitive changes, and depression. Laboratory abnormalities include the reduction of myeloid cells, including granulocytes, platelets and to a lesser extent, red blood cells. These changes in blood cell counts rarely lead to any significant clinical sequelae. In addition, increases in triglyceride concentrations and elevations in serum alanine and aspartate aminotransferase concentration have been observed. Finally, thyroid abnormalities have been reported. These thyroid abnormalities are usually reversible after cessation of interferon therapy and can be controlled with appropriate medication while on therapy. Miscellaneous side effects include nausea, diarrhea, abdominal and back pain, pruritus, alopecia, and rhinorrhea. In general, most side effects will abate after 4 to 8 weeks of therapy (Dushieko *et al.*, *supra*).

Lamivudine (3TC®) is a nucleoside analogue, which is a very potent and specific inhibitor of HBV DNA synthesis. Lamivudine has recently been approved for the treatment of chronic Hepatitis B. Unlike treatment with interferon, treatment with 3TC® does not eliminate the HBV from the patient. Rather, viral replication is controlled and chronic administration results in improvements in liver histology in over 50% of patients. Phase III studies with 3TC®, showed that treatment for one year was associated with reduced liver inflammation and a delay in scarring of the liver. In addition, patients treated with Lamivudine (100mg per day) had a 98 percent reduction in hepatitis B DNA and a significantly higher rate of seroconversion, suggesting disease improvements after completion of therapy. However, stopping of therapy resulted in a reactivation of HBV replication in most patients. In addition recent reports have documented 3TC® resistance in approximately 30% of patients.

Current therapies for treating HBV infection, including interferon and nucleoside analogues, are only partially effective. In addition, drug resistance to nucleoside analogues is now emerging, making treatment of chronic Hepatitis B more difficult. Thus, a need exists for effective treatment of this disease that utilizes antiviral modulators that work by mechanisms other than those currently utilized in the treatment of both acute and chronic hepatitis B infections.

Welch *et al.*, *Gene Therapy* 1996 3(11): 994-1001 describe *in vitro* and *in vivo* studies with two vector expressed hairpin ribozymes targeted against hepatitis C virus.

Sakamoto *et al.*, *J. Clinical Investigation* 1996 98(12): 2720-2728 describe intracellular cleavage of hepatitis C virus RNA and inhibition of viral protein translation by certain vector expressed hammerhead ribozymes.

Lieber *et al.*, *J. Virology* 1996 70(12): 8782-8791 describe elimination of hepatitis C virus RNA in infected human hepatocytes by adenovirus-mediated expression of certain hammerhead ribozymes.

Ohkawa *et al.*, 1997, *J. Hepatology*, 27; 78-84, describe *in vitro* cleavage of HCV RNA and inhibition of viral protein translation using certain *in vitro* transcribed hammerhead ribozymes.

Barber *et al.*, International PCT Publication No. *WO 97/32018*, describe the use of an adenovirus vector to express certain anti-hepatitis C virus hairpin ribozymes.

Kay *et al.*, International PCT Publication No. *WO 96/18419*, describe certain recombinant adenovirus vectors to express anti-HCV hammerhead ribozymes.

Yamada *et al.*, Japanese Patent Application No. *JP 07231784* describe a specific poly-(L)-lysine conjugated hammerhead ribozyme targeted against HCV.

Draper, U.S. Patent Nos. 5,610,054 and 5,869,253, describes enzymatic nucleic acid molecules capable of inhibiting replication of HCV.

Macejak *et al.*, 2000, *Hepatology*, 31, 769-776, describe enzymatic nucleic acid molecules capable of inhibiting replication of HCV.

Weifeng and Torrence, 1997, *Nucleosides and Nucleotides*, 16, 7-9, describe the synthesis of 2-5A antisense chimeras with various non-nucleoside components.

Torrence *et al.*, US patent No. 5,583,032 describe targeted cleavage of RNA using an antisense oligonucleotide linked to a 2',5'-oligoadenylate activator of RNase L.

Suhadolnik and Pfeleiderer, US patent Nos. 5,863,905; 5,700,785; 5,643,889; 5,556,840; 5,550,111; 5,405,939; 5,188,897; 4,924,624; and 4,859,768 describe specific internucleotide phosphorothioate 2',5'-oligoadenylates and 2',5'-oligoadenylate conjugates.

Budowsky *et al.*, US patent No. 5,962,431 describe a method of treating papillomavirus using specific 2',5'-oligoadenylates.

Torrence *et al.*, International PCT publication No. *WO 00/14219*, describe specific peptide nucleic acid 2',5'-oligoadenylate chimeric molecules.

Stinchcomb *et al.*, US patent No. 5,817,796, describe C-myb ribozymes having 2'-5'-Linked Adenylate Residues.

Draper, US patent No. 6,017,756, describes the use of ribozymes for the inhibition of Hepatitis B Virus.

Passman *et al.*, 2000, *Biochem. Biophys. Res. Commun.*, 268(3), 728-733.; Gan *et al.*, 1998, *J. Med. Coll. PLA*, 13(3), 157-159.; Li *et al.*, 1999, *Jiefangjun Yixue Zazhi*, 24(2), 99-101.; Putlitz *et al.*, 1999, *J. Virol.*, 73(7), 5381-5387.; Kim *et al.*, 1999, *Biochem. Biophys. Res. Commun.*, 257(3), 759-765.; Xu *et al.*, 1998, *Bingdu Xuebao*, 14(4), 365-369.; Welch *et al.*, 1997, *Gene Ther.*, 4(7), 736-743.; Goldenberg *et al.*, 1997, International PCT publication No. WO 97/08309, Wands *et al.*, 1997, *J. of Gastroenterology and Hepatology*, 12(suppl.), S354-S369.; Ruiz *et al.*, 1997, *BioTechniques*, 22(2), 338-345.; Gan *et al.*, 1996, *J. Med. Coll. PLA*, 11(3), 171-175.; Beck and Nassal, 1995, *Nucleic Acids Res.*, 23(24), 4954-62.; Goldenberg, 1995, International PCT publication No. WO 95/22600.; Xu *et al.*, 1993, *Bingdu Xuebao*, 9(4), 331-6.; Wang *et al.*, 1993, *Bingdu Xuebao*, 9(3), 278-80, all describe ribozymes that are targeted to cleave a specific HBV target site.

Hunt *et al.*, US patent No. 5,859,226, describes specific non-naturally occurring oligonucleotide decoys intended to inhibit the expression of MHC-II genes through binding of the RF-X transcription factor, that can inhibit the expression of certain HBV and CMV viral proteins.

Kao *et al.*, International PCT Publication No. WO 00/04141, describes linear single stranded nucleic acid molecules capable of specifically binding to viral polymerases and inhibiting the activity of the viral polymerase.

Lu, International PCT Publication No. WO 99/20641, describes specific triplex-forming oligonucleotides used in treating HBV infection.

SUMMARY OF THE INVENTION

This invention relates to enzymatic nucleic acid molecules that can disrupt the function of RNA species of hepatitis B virus (HBV), hepatitis C virus (HCV) and/or those RNA species encoded by HBV or HCV. In particular, applicant provides enzymatic nucleic acid molecules capable of specifically cleaving HBV RNA or HCV RNA and describes the selection and function thereof. Such enzymatic nucleic acid molecules can be used to treat diseases and disorders associated with HBV and HCV infection.

In one embodiment, the invention features an enzymatic nucleic acid molecule that specifically cleaves RNA derived from hepatitis B virus (HBV), wherein the enzymatic nucleic acid molecule comprises sequence defined as Seq. ID No. 10887.

In another embodiment, the invention features a composition comprising an enzymatic nucleic acid molecule of the invention and a pharmaceutically acceptable carrier.

In another embodiment, the invention features a mammalian cell, for example a human cell, comprising an enzymatic nucleic acid molecule contemplated by the invention.

5 In one embodiment, the invention features a method for the treatment of cirrhosis, liver failure or hepatocellular carcinoma comprising administering to a patient an enzymatic nucleic acid molecule of the invention under conditions suitable for the treatment.

10 In another embodiment, the invention features a method for the treatment of a patient having a condition associated with HBV and/or HCV infection, comprising contacting cells of said patient with an enzymatic nucleic acid molecule of the invention.

15 In another embodiment, the invention features a method for the treatment of a patient having a condition associated with HBV and/or HCV infection, comprising contacting cells of said patient with an enzymatic nucleic acid molecule of the invention and further comprising the use of one or more drug therapies, for example, type I interferon or 3TC® (lamivudine), under conditions suitable for said treatment. In another embodiment, the other therapy is administered simultaneously with or separately from the enzymatic nucleic acid molecule.

20 In another embodiment, the invention features a method for inhibiting HBV and/or HCV replication in a mammalian cell comprising administering to the cell an enzymatic nucleic acid molecule of the invention under conditions suitable for the inhibition.

In yet another embodiment, the invention features a method of cleaving a separate HBV and/or HCV RNA comprising contacting an enzymatic nucleic acid molecule of the invention with the separate RNA under conditions suitable for the cleavage of the separate RNA.

25 In one embodiment, cleavage by an enzymatic nucleic acid molecule of the invention is carried out in the presence of a divalent cation, for example Mg²⁺.

In another embodiment, the enzymatic nucleic acid molecule of the invention is chemically synthesized.

30 In another embodiment, the type I interferon contemplated by the invention is interferon alpha, interferon beta, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, polyethylene glycol consensus interferon.

In one embodiment, the invention features a composition comprising type I interferon and an enzymatic nucleic acid molecule of the invention and a pharmaceutically acceptable carrier.

5 In another embodiment, the invention features a method of administering to a cell, for example a mammalian cell or human cell, an enzymatic nucleic acid molecule of the invention independently or in conjunction with other therapeutic compounds, such as type I interferon or 3TC® (lamivudine), comprising contacting the cell with the enzymatic nucleic acid molecule under conditions suitable for the administration.

10 In another embodiment, administration of an enzymatic nucleic acid molecule of the invention is in the presence of a delivery reagent, for example a lipid, cationic lipid, phospholipid, or liposome.

In another embodiment, the invention features novel nucleic acid-based techniques such as enzymatic nucleic acid molecules and antisense molecules and methods for their use to down regulate or inhibit the expression of HBV RNA and/or replication of HBV.

15 In another embodiment, the invention features novel nucleic acid-based techniques such as enzymatic nucleic acid molecules and antisense molecules and methods for their use to down regulate or inhibit the expression of HCV RNA and/or replication of HCV.

20 In one embodiment, the invention features the use of one or more of the enzymatic nucleic acid-based techniques to down-regulate or inhibit the expression of the genes encoding HBV and/or HCV viral proteins. Specifically, the invention features the use of enzymatic nucleic acid-based techniques to specifically down-regulate or inhibit the expression of the HBV and/or HCV viral genome.

25 In another embodiment, the invention features nucleic acid-based inhibitors (*e.g.*, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, triplex DNA, decoys, siRNA, aptamers, and antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or inhibit the expression of RNA (*e.g.*, HBV and/or HCV) capable of progression and/or maintenance of hepatitis, hepatocellular carcinoma, cirrhosis, and/or liver failure.

30 In one embodiment, nucleic acid molecules of the invention are used to treat HBV infected cells or an HBV infected patient wherein the HBV is resistant or the patient does not respond to treatment with 3TC® (Lamivudine), either alone or in combination with other therapies under conditions suitable for the treatment.

In yet another embodiment, the invention features the use of an enzymatic nucleic acid molecule, preferably in the hammerhead, NCH (Inozyme), G-cleaver, amberzyme, zinzyme, and/or DNAzyme motif, to inhibit the expression of HBV and/or HCV RNA.

The enzymatic nucleic acid molecules described herein exhibit a high degree of specificity for only the viral mRNA in infected cells. Nucleic acid molecules of the instant invention targeted to highly conserved sequence regions allow the treatment of many strains of human HBV and/or HCV with a single compound. No treatment presently exists which specifically attacks expression of the viral gene(s) that are responsible for transformation of hepatocytes by HBV and/or HCV.

The enzymatic nucleic acid-based modulators of HBV and HCV expression are useful for the prevention of the diseases and conditions including HBV and HCV infection, hepatitis, cancer, cirrhosis, liver failure, and any other diseases or conditions that are related to the levels of HBV and/or HCV in a cell or tissue.

Preferred target sites are genes required for viral replication, a non-limiting example includes genes for protein synthesis, such as the 5' most 1500 nucleotides of the HBV pregenomic mRNAs. For sequence references, see Renbao *et al.*, 1987, *Sci. Sin.*, 30, 507. This region controls the translational expression of the core protein (C), X protein (X) and DNA polymerase (P) genes and plays a role in the replication of the viral DNA by serving as a template for reverse transcriptase. Disruption of this region in the RNA results in deficient protein synthesis as well as incomplete DNA synthesis (and inhibition of transcription from the defective genomes). Targeting sequences 5' of the encapsidation site can result in the inclusion of the disrupted 3' RNA within the core virion structure and targeting sequences 3' of the encapsidation site can result in the reduction in protein expression from both the 3' and 5' fragments.

Alternative regions outside of the 5' most 1500 nucleotides of the pregenomic mRNA also make suitable targets for enzymatic nucleic acid mediated inhibition of HBV replication. Such targets include the mRNA regions that encode the viral S gene. Selection of particular target regions will depend upon the secondary structure of the pregenomic mRNA. Targets in the minor mRNAs can also be used, especially when folding or accessibility assays in these other RNAs reveal additional target sequences that are unavailable in the pregenomic mRNA species.

A desirable target in the pregenomic RNA is a proposed bipartite stem-loop structure in the 3'-end of the pregenomic RNA which is believed to be critical for viral replication (Kidd and Kidd-Ljunggren, 1996. *Nuc. Acid Res.* 24:3295-3302). The 5'end of the HBV pregenomic RNA carries a *cis*-acting encapsidation signal, which has inverted repeat

sequences that are thought to form a bipartite stem-loop structure. Due to a terminal redundancy in the pregenomic RNA, the putative stem-loop also occurs at the 3'-end. While it is the 5' copy which functions in polymerase binding and encapsidation, reverse transcription actually begins from the 3' stem-loop. To start reverse transcription, a 4 nt primer which is covalently attached to the polymerase is made, using a bulge in the 5' encapsidation signal as template. This primer is then shifted, by an unknown mechanism, to the DR1 primer binding site in the 3' stem-loop structure, and reverse transcription proceeds from that point. The 3' stem-loop, and especially the DR1 primer binding site, appear to be highly effective targets for ribozyme intervention.

Sequences of the pregenomic RNA are shared by the mRNAs for surface, core, polymerase, and X proteins. Due to the overlapping nature of the HBV transcripts, all share a common 3'-end. Enzymatic nucleic acids targeting of this common 3'-end will thus cleave the pregenomic RNA as well as all of the mRNAs for surface, core, polymerase and X proteins.

At least seven basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds in *trans* (and thus can cleave other RNA molecules) under physiological conditions. **Table I** summarizes some of the characteristics of these enzymatic RNA molecules. In general, enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets. Thus, a single enzymatic nucleic acid molecule is able to cleave many molecules of target RNA. In addition, the enzymatic nucleic acid is a highly specific inhibitor of gene expression, with the specificity of inhibition depending not only on the base-pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a an enzymatic nucleic acid molecule.

The enzymatic nucleic acid molecules that cleave the specified sites in HBV-specific RNAs represent a novel therapeutic approach to treat a variety of pathologic indications, including, HBV infection, hepatitis, hepatocellular carcinoma, tumorigenesis, cirrhosis, liver failure and other conditions related to the level of HBV.

In one of the preferred embodiments of the inventions described herein, the enzymatic nucleic acid molecule is formed in a hammerhead or hairpin motif, but can also be formed in the motif of a hepatitis delta virus, group I intron, group II intron or RNase P RNA (in association with an RNA guide sequence), *Neurospora* VS RNA, DNAzymes, NCH cleaving motifs, or G-cleavers. Examples of such hammerhead motifs are described by Dreyfus, *supra*, Rossi *et al.*, 1992, *AIDS Research and Human Retroviruses* 8, 183. Examples of hairpin motifs are described by Hampel *et al.*, EP0360257, Hampel and Tritz, 1989 *Biochemistry* 28, 4929, Feldstein *et al.*, 1989, *Gene* 82, 53, Haseloff and Gerlach, 1989, *Gene*, 82, 43, Hampel *et al.*, 1990 *Nucleic Acids Res.* 18, 299; and Chowrira & McSwiggen, US. Patent No. 5,631,359. The hepatitis delta virus motif is described by Perrotta and Been, 1992 *Biochemistry* 31, 16. The RNase P motif is described by Guerrier-Takada *et al.*, 1983 *Cell* 35, 849; Forster and Altman, 1990, *Science* 249, 783; and Li and Altman, 1996, *Nucleic Acids Res.* 24, 835. The *Neurospora* VS RNA ribozyme motif is described by Collins (Saville and Collins, 1990 *Cell* 61, 685-696; Saville and Collins, 1991 *Proc. Natl. Acad. Sci. USA* 88, 8826-8830; Collins and Olive, 1993 *Biochemistry* 32, 2795-2799; and Guo and Collins, 1995, *EMBO. J.* 14, 363). Group II introns are described by Griffin *et al.*, 1995, *Chem. Biol.* 2, 761; Michels and Pyle, 1995, *Biochemistry* 34, 2965; and Pyle *et al.*, International PCT Publication No. WO 96/22689. The Group I intron is described by Cech *et al.*, U.S. Patent 4,987,071. DNAzymes are described by Usman *et al.*, International PCT Publication No. WO 95/11304; Chartrand *et al.*, 1995, *NAR* 23, 4092; Breaker *et al.*, 1995, *Chem. Bio.* 2, 655; and Santoro *et al.*, 1997, *PNAS* 94, 4262. NCH cleaving motifs are described in Ludwig & Sproat, International PCT Publication No. WO 98/58058; and G-cleavers are described in Kore *et al.*, 1998, *Nucleic Acids Research* 26, 4116-4120 and Eckstein *et al.*, International PCT Publication No. WO 99/16871. Additional motifs include the Aptazyme (Breaker *et al.*, WO 98/43993), Amberzyme (Class I motif; **Figure 3**; Beigelman *et al.*, International PCT publication No. WO 99/55857) and Zinzyme (Beigelman *et al.*, International PCT publication No. WO 99/55857), all these references are incorporated by reference herein in their totalities, including drawings and can also be used in the present invention. These specific motifs are not limiting in the invention and those skilled in the art will recognize that all that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule (Cech *et al.*, U.S. Patent No. 4,987,071).

In preferred embodiments of the present invention, a nucleic acid molecule, *e.g.*, an antisense molecule, a triplex DNA, or a ribozyme, is 13 to 100 nucleotides in length, *e.g.*, in specific embodiments 35, 36, 37, or 38 nucleotides in length (*e.g.*, for particular ribozymes or antisense). In particular embodiments, the nucleic acid molecule is 15-100, 17-100, 20-100,

21-100, 23-100, 25-100, 27-100, 30-100, 32-100, 35-100, 40-100, 50-100, 60-100, 70-100, or 80-100 nucleotides in length. Instead of 100 nucleotides being the upper limit on the length ranges specified above, the upper limit of the length range can be, for example, 30, 40, 50, 60, 70, or 80 nucleotides. Thus, for any of the length ranges, the length range for particular
 5 embodiments has lower limit as specified, with an upper limit as specified which is greater than the lower limit. For example, in a particular embodiment, the length range can be 35-50 nucleotides in length. All such ranges are expressly included. Also in particular embodiments, a nucleic acid molecule can have a length which is any of the lengths specified above, for example, 21 nucleotides in length.

10 Exemplary enzymatic nucleic acid molecules of the invention targeting HBV are shown in **Tables V-XI**. For example, enzymatic nucleic acid molecules of the invention are preferably between 15 and 50 nucleotides in length, more preferably between 25 and 40 nucleotides in length, *e.g.*, 34, 36, or 38 nucleotides in length (for example see Jarvis *et al.*, 1996, *J. Biol. Chem.*, 271, 29107-29112). Exemplary DNAzymes of the invention are
 15 preferably between 15 and 40 nucleotides in length, more preferably between 25 and 35 nucleotides in length, *e.g.*, 29, 30, 31, or 32 nucleotides in length (see for example Santoro *et al.*, 1998, *Biochemistry*, 37, 13330-13342; Chartrand *et al.*, 1995, *Nucleic Acids Research*, 23, 4092-4096). Exemplary antisense molecules of the invention are preferably between 15 and 75 nucleotides in length, more preferably between 20 and 35 nucleotides in length, *e.g.*,
 20 25, 26, 27, or 28 nucleotides in length (see for example Woolf *et al.*, 1992, *PNAS*, 89, 7305-7309; Milner *et al.*, 1997, *Nature Biotechnology*, 15, 537-541). Exemplary triplex forming oligonucleotide molecules of the invention are preferably between 10 and 40 nucleotides in length, more preferably between 12 and 25 nucleotides in length, *e.g.*, 18, 19, 20, or 21 nucleotides in length (see for example Maher *et al.*, 1990, *Biochemistry*, 29, 8820-8826;
 25 Strobel and Dervan, 1990, *Science*, 249, 73-75). Those skilled in the art will recognize that all that is required is for the nucleic acid molecule are of length and conformation sufficient and suitable for the nucleic acid molecule to catalyze a reaction contemplated herein. The length of the nucleic acid molecules of the instant invention are not limiting within the general limits stated.

30 In a preferred embodiment, the invention provides a method for producing a class of nucleic acid-based gene inhibiting agents which exhibit a high degree of specificity for the RNA of a desired target. For example, the enzymatic nucleic acid molecule is preferably targeted to a highly conserved sequence region of target RNAs encoding HBV proteins (specifically HBV RNA) such that specific treatment of a disease or condition can be
 35 provided with either one or several nucleic acid molecules of the invention. Such nucleic acid molecules can be delivered exogenously to specific tissue or cellular targets as required.

Alternatively, the nucleic acid molecules (*e.g.*, ribozymes and antisense) can be expressed from DNA and/or RNA vectors that are delivered to specific cells.

The enzymatic nucleic acid-based inhibitors of HBV expression are useful for the prevention of the diseases and conditions including HBV infection, hepatitis, cancer, cirrhosis, liver failure, and any other diseases or conditions that are related to the levels of HBV in a cell or tissue.

The nucleic acid-based inhibitors of the invention are added directly, or can be complexed with cationic lipids, packaged within liposomes, or otherwise delivered to target cells or tissues. The nucleic acid or nucleic acid complexes can be locally administered to relevant tissues *ex vivo*, or *in vivo* through injection, infusion pump or stent, with or without their incorporation in biopolymers. In preferred embodiments, the enzymatic nucleic acid HBV inhibitors comprise sequences, which are complementary to the substrate sequences in **Tables IV to XI**. Examples of such enzymatic nucleic acid molecules also are shown in **Tables V to XI**. Examples of such enzymatic nucleic acid molecules consist essentially of sequences defined in these tables.

In yet another embodiment, the invention features antisense nucleic acid molecules including sequences complementary to the HBV substrate sequences shown in **Tables IV to XI**. Such nucleic acid molecules can include sequences as shown for the binding arms of the enzymatic nucleic acid molecules in **Tables V to XI**. Similarly, triplex molecules can be provided targeted to the corresponding DNA target regions, and regions containing the DNA equivalent of a target sequence or a sequence complementary to the specified target (substrate) sequence. Typically, antisense molecules are complementary to a target sequence along a single contiguous sequence of the antisense molecule. However, in certain embodiments, an antisense molecule can bind to substrate such that the substrate molecule forms a loop, and/or an antisense molecule can bind such that the antisense molecule forms a loop. Thus, the antisense molecule can be complementary to two (or even more) non-contiguous substrate sequences or two (or even more) non-contiguous sequence portions of an antisense molecule can be complementary to a target sequence or both.

By “consists essentially of” is meant that the active nucleic acid molecule of the invention, for example, an enzymatic nucleic acid molecule, contains an enzymatic center or core equivalent to those in the examples, and binding arms able to bind RNA such that cleavage at the target site occurs. Other sequences can be present which do not interfere with such cleavage. Thus, a core region can, for example, include one or more loops, stem-loop structure, or linker which does not prevent enzymatic activity. Thus, the underlined regions in the sequences in **Tables V and VI** can be such a loop, stem-loop, nucleotide linker, and/or non-nucleotide linker and can be represented generally as sequence “X”. For example, a core

sequence for a hammerhead enzymatic nucleic acid can comprise a conserved sequence, such as 5'-CUGAUGAG-3' and 5'-CGAA-3' connected by "X", where X is 5'-GCCGUUAGGC-3' (SEQ ID NO. 16201), or any other Stem II region known in the art, or a nucleotide and/or non-nucleotide linker. Similarly, for other nucleic acid molecules of the instant invention, such as Inozyme, G-cleaver, amberzyme, zinzyme, DNAzyme, antisense, 2-5A antisense, triplex forming nucleic acid, and decoy nucleic acids, other sequences or non-nucleotide linkers can be present that do not interfere with the function of the nucleic acid molecule.

In another aspect of the invention, enzymatic nucleic acids or antisense molecules that interact with target RNA molecules and inhibit HBV (specifically HBV RNA) activity are expressed from transcription units inserted into DNA or RNA vectors. The recombinant vectors are preferably DNA plasmids or viral vectors. Enzymatic nucleic acid or antisense expressing viral vectors can be constructed based on, but not limited to, adeno-associated virus, retrovirus, adenovirus, or alphavirus. Preferably, the recombinant vectors capable of expressing the enzymatic nucleic acids or antisense are delivered as described above, and persist in target cells. Alternatively, viral vectors can be used that provide for transient expression of enzymatic nucleic acids or antisense. Such vectors can be repeatedly administered as necessary. Once expressed, the enzymatic nucleic acids or antisense bind to the target RNA and inhibit its function or expression. Delivery of enzymatic nucleic acids or antisense expressing vectors can be systemic, such as by intravenous or intramuscular administration, by administration to target cells ex-planted from the patient followed by reintroduction into the patient, or by any other means that allow for introduction into the desired target cell. Antisense DNA can be expressed via the use of a single stranded DNA intracellular expression vector.

In another embodiment, the invention features nucleic acid-based inhibitors (*e.g.*, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, triplex DNA, decoys, aptamers, siRNA, antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or inhibit the expression of RNA (*e.g.*, HBV) capable of progression and/or maintenance of liver disease and failure.

In another embodiment, the invention features nucleic acid-based techniques (*e.g.*, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, triplex DNA, decoys, aptamers, siRNA, antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or inhibit the expression of HBV RNA expression.

In other embodiments, the invention features a method for the analysis of HBV proteins. This method is useful in determining the efficacy of HBV inhibitors. Specifically, the instant invention features an assay for the analysis of HBsAg proteins and secreted

alkaline phosphatase (SEAP) control proteins to determine the efficacy of agents used to modulate HBV expression.

The method consists of coating a micro-titer plate with an antibody such as anti-HBsAg Mab (for example, Biostride B88-95-31ad,ay) at 0.1 to 10 µg/ml in a buffer (for example, carbonate buffer, such as Na₂CO₃ 15 mM, NaHCO₃ 35 mM, pH 9.5) at 4°C overnight. The microtiter wells are then washed with PBST or the equivalent thereof, (for example, PBS, 0.05% Tween 20) and blocked for 0.1-24 hr at 37° C with PBST, 1% BSA or the equivalent thereof. Following washing as above, the wells are dried (for example, at 37° C for 30 min). Biotinylated goat anti-HBsAg or an equivalent antibody (for example, Accurate YVS1807) is diluted (for example at 1:1000) in PBST and incubated in the wells (for example, 1 hr. at 37° C). The wells are washed with PBST (for example, 4x). A conjugate, (for example, Streptavidin/Alkaline Phosphatase Conjugate, Pierce 21324) is diluted to 10-10,000 ng/ml in PBST, and incubated in the wells (for example, 1 hr. at 37° C). After washing as above, a substrate (for example, p-nitrophenyl phosphate substrate, Pierce 37620) is added to the wells, which are then incubated (for example, 1 hr. at 37° C). The optical density is then determined (for example, at 405 nm). SEAP levels are then assayed, for example, using the Great EscAPe® Detection Kit (Clontech K2041-1), as per the manufacturers instructions. In the above example, incubation times and reagent concentrations can be varied to achieve optimum results, a non-limiting example is described in Example 6.

Comparison of this HBsAg ELISA method to a commercially available assay from World Diagnostics, Inc. 15271 NW 60th Ave, #201, Miami Lakes, FL 33014 (305) 827-3304 (Cat. No. EL10018) demonstrates an increase in sensitivity (signal:noise) of 3-20 fold.

This invention also relates to nucleic acid molecules directed to disrupt the function of HBV reverse transcriptase. In addition, the invention relates to nucleic acid molecules directed to disrupt the function of the Enhancer I core region of the HBV genomic DNA. In particular, the present invention describes the selection and function of nucleic acid molecules, such as decoys and aptamers, capable of specifically binding to the HBV reverse transcriptase (pol) primer and modulating reverse transcription of the HBV pregenomic RNA. In another embodiment, the present invention relates to nucleic acid molecules, such as decoys, antisense and aptamers, capable of specifically binding to the HBV reverse transcriptase (pol) and modulating reverse transcription of the HBV pregenomic RNA. In yet another embodiment, the present invention relates to nucleic acid molecules capable of specifically binding to the HBV Enhancer I core region and modulating transcription of the HBV genomic DNA. The invention further relates to allosteric enzymatic nucleic acid molecules or “allozymes” that are used to modulate HBV gene expression. Such allozymes are active in the presence of HBV-derived nucleic acids, peptides, and/or proteins such as

HBV reverse transcriptase and/or a HBV reverse transcriptase primer sequence, thereby allowing the allozyme to selectively cleave a sequence of HBV DNA or RNA. Allozymes of the invention are also designed to be active in the presence of HBV Enhancer I sequences and/or mutant HBV Enhancer I sequences, thereby allowing the allozyme to selectively
5 cleave a sequence of HBV DNA or RNA. These nucleic acid molecules can be used to treat diseases and disorders associated with HBV infection.

In one embodiment, the invention features a nucleic acid decoy molecule that specifically binds the hepatitis B virus (HBV) reverse transcriptase primer sequence. In another embodiment, the invention features a nucleic acid decoy molecule that specifically
10 binds the hepatitis B virus (HBV) reverse transcriptase. In yet another embodiment, the invention features a nucleic acid decoy molecule that specifically binds to the HBV Enhancer I core sequence.

In one embodiment, the invention features a nucleic acid aptamer that specifically binds the hepatitis B virus (HBV) reverse transcriptase primer. In another embodiment, the
15 invention features a nucleic acid aptamer that specifically binds the hepatitis B virus (HBV) reverse transcriptase. In yet another embodiment, the invention features a nucleic acid aptamer molecule that specifically binds to the HBV Enhancer I core sequence.

In one embodiment, the invention features an allozyme that specifically binds the hepatitis B virus (HBV) reverse transcriptase primer. In another embodiment, the invention
20 features an allozyme that specifically binds the hepatitis B virus (HBV) reverse transcriptase. In yet another embodiment, the invention features an allozyme that specifically binds to the HBV Enhancer I core sequence.

In yet another embodiment, the invention features a nucleic acid molecule, for example a triplex forming nucleic acid molecule or antisense nucleic acid molecule, that binds the
25 hepatitis B virus (HBV) reverse transcriptase primer. In another embodiment, the invention features a triplex forming nucleic acid molecule or antisense nucleic acid molecule that specifically binds the hepatitis B virus (HBV) reverse transcriptase. In yet another embodiment, the invention features a triplex forming nucleic acid molecule or antisense nucleic acid molecule that specifically binds to the HBV Enhancer I core sequence.

In another embodiment, a nucleic acid molecule of the invention binds to Hepatocyte Nuclear Factor 3 (HNF3) and/or Hepatocyte Nuclear Factor 4 (HNF4) binding sequence within the HBV Enhancer I region of HBV genomic DNA, for example the plus strand and/or
30 minus strand DNA of the Enhancer I region, and blocks the binding of HNF3 and/or HNF4 to the Enhancer I region.

In another embodiment, the nucleic acid molecule of the invention comprises a sequence having (UUCA)_n domain, where n is an integer from 1-10. In another embodiment, the nucleic acid molecules of the invention comprise the sequence of SEQ. ID NOs: 11216 - 11342.

5 In another embodiment, the invention features a composition comprising a nucleic acid molecule of the invention and a pharmaceutically acceptable carrier. In another embodiment, the invention features a mammalian cell, for example a human cell, including a nucleic acid molecule contemplated by the invention.

10 In one embodiment, the invention features a method for treatment of HBV infection, cirrhosis, liver failure, or hepatocellular carcinoma, comprising administering to a patient a nucleic acid molecule of the invention under conditions suitable for the treatment.

In another embodiment, the invention features a method for the treatment of a patient having a condition associated with HBV infection comprising contacting cells of said patient with a nucleic acid molecule of the invention under conditions suitable for such treatment. In
15 another embodiment, the invention features a method for the treatment of a patient having a condition associated with HBV infection comprising contacting cells of said patient with a nucleic acid molecule of the invention, and further comprising the use of one or more drug therapies, for example type I interferon or 3TC® (lamivudine), under conditions suitable for said treatment. In another embodiment, the other therapy is administered simultaneously
20 with or separately from the nucleic acid molecule.

In another embodiment, the invention features a method for modulating HBV replication in a mammalian cell comprising administering to the cell a nucleic acid molecule of the invention under conditions suitable for the modulation.

25 In yet another embodiment, the invention features a method of modulating HBV reverse transcriptase activity comprising contacting a nucleic acid molecule of the invention, for example a decoy or aptamer, with HBV reverse transcriptase under conditions suitable for the modulating of the HBV reverse transcriptase activity.

In another embodiment, the invention features a method of modulating HBV transcription comprising contacting a nucleic molecule of the invention with a HBV
30 Enhancer I sequence under conditions suitable for the modulation of HBV transcription.

In one embodiment, a nucleic acid molecule of the invention, for example a decoy or aptamer, is chemically synthesized. In another embodiment, the nucleic acid molecule of the invention comprises at least one nucleic acid sugar modification. In yet another embodiment, the nucleic acid molecule of the invention comprises at least one nucleic acid base

modification. In another embodiment, the nucleic acid molecule of the invention comprises at least one nucleic acid backbone modification.

5 In another embodiment, the nucleic acid molecule of the invention comprises at least one 2'-O-alkyl, 2'-alkyl, 2'-alkoxylalkyl, 2'-alkylthioalkyl, 2'-amino, 2'-O-amino, or 2'-halo modification and/or any combination thereof with or without 2'-deoxy and/or 2'-ribo nucleotides. In yet another embodiment, the nucleic acid molecule of the invention comprises all 2'-O-alkyl nucleotides, for example, all 2'-O-allyl nucleotides.

In one embodiment, the nucleic acid molecule of the invention comprises a 5'-cap, 3'-cap, or 5'-3' cap structure, for example an abasic or inverted abasic moiety.

10 In another embodiment, the nucleic acid molecule of the invention is a linear nucleic acid molecule. In another embodiment, the nucleic acid molecule of the invention is a linear nucleic acid molecule that can optionally form a hairpin, loop, stem-loop, or other secondary structure. In yet another embodiment, the nucleic acid molecule of the invention is a circular nucleic acid molecule.

15 In one embodiment, the nucleic acid molecule of the invention is a single stranded oligonucleotide. In another embodiment, the nucleic acid molecule of the invention is a double-stranded oligonucleotide.

20 In one embodiment, the nucleic acid molecule of the invention comprises an oligonucleotide having between about 3 and about 100 nucleotides. In another embodiment, the nucleic acid molecule of the invention comprises an oligonucleotide having between about 3 and about 24 nucleotides. In another embodiment, the nucleic acid molecule of the invention comprises an oligonucleotide having between about 4 and about 16 nucleotides.

25 The nucleic acid decoy molecules and/or aptamers that bind to a reverse transcriptase and/or reverse transcriptase primer and therefore inactivate the reverse transcriptase, represent a novel therapeutic approach to treat a variety of pathologic indications, including, viral infection such as HBV infection, hepatitis, hepatocellular carcinoma, tumorigenesis, cirrhosis, liver failure and others.

30 The nucleic acid molecules that bind to a HBV Enhancer I sequence and therefore inactivate HBV transcription, represent a novel therapeutic approach to treat a variety of pathologic indications, including viral infection such as HBV infection, hepatitis, hepatocellular carcinoma, tumorigenesis, cirrhosis, liver failure and others conditions associated with the level of HBV.

In one embodiment of the present invention, a decoy nucleic acid molecule of the invention is 4 to 50 nucleotides in length, in specific embodiments about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 nucleotides in length. In another embodiment, a non-decoy nucleic acid molecule, *e.g.*, an antisense molecule, a triplex DNA, or a ribozyme, is 13 to 100 nucleotides in length, *e.g.*, in specific embodiments 35, 36, 37, or 38 nucleotides in length (*e.g.*, for particular ribozymes or antisense). In particular embodiments, the nucleic acid molecule is 15-100, 17-100, 20-100, 21-100, 23-100, 25-100, 27-100, 30-100, 32-100, 35-100, 40-100, 50-100, 60-100, 70-100, or 80-100 nucleotides in length. Instead of 100 nucleotides being the upper limit on the length ranges specified above, the upper limit of the length range can be, for example, 30, 40, 50, 60, 70, or 80 nucleotides. Thus, for any of the length ranges, the length range for particular embodiments has lower limit as specified, with an upper limit as specified which is greater than the lower limit. For example, in a particular embodiment, the length range can be 35-50 nucleotides in length. All such ranges are expressly included. Also in particular embodiments, a nucleic acid molecule can have a length which is any of the lengths specified above, for example, 21 nucleotides in length.

Exemplary nucleic acid decoy molecules of the invention are shown in **Table XIV**. Exemplary synthetic nucleic acid molecules of the invention are shown in **Table XV**. For example, decoy molecules of the invention are between 4 and 40 nucleotides in length. Exemplary decoys of the invention are 4, 8, 12, or 16 nucleotides in length. In an additional example, enzymatic nucleic acid molecules of the invention are preferably between 15 and 50 nucleotides in length, more preferably between 25 and 40 nucleotides in length, *e.g.*, 34, 36, or 38 nucleotides in length (for example see Jarvis *et al.*, 1996, *J. Biol. Chem.*, 271, 29107-29112). Exemplary DNAzymes of the invention are preferably between 15 and 40 nucleotides in length, more preferably between 25 and 35 nucleotides in length, *e.g.*, 29, 30, 31, or 32 nucleotides in length (see for example Santoro *et al.*, 1998, *Biochemistry*, 37, 13330-13342; Chartrand *et al.*, 1995, *Nucleic Acids Research*, 23, 4092-4096). Exemplary antisense molecules of the invention are preferably between 15 and 75 nucleotides in length, more preferably between 20 and 35 nucleotides in length, *e.g.*, 25, 26, 27, or 28 nucleotides in length (see for example Woolf *et al.*, 1992, *PNAS*, 89, 7305-7309; Milner *et al.*, 1997, *Nature Biotechnology*, 15, 537-541). Exemplary triplex forming oligonucleotide molecules of the invention are preferably between 10 and 40 nucleotides in length, more preferably between 12 and 25 nucleotides in length, *e.g.*, 18, 19, 20, or 21 nucleotides in length (see for example Maher *et al.*, 1990, *Biochemistry*, 29, 8820-8826; Strobel and Dervan, 1990, *Science*, 249, 73-75). Those skilled in the art will recognize that all that is required is that the nucleic acid molecule is of length and conformation sufficient and suitable for the nucleic acid molecule to catalyze a reaction contemplated herein. The length of the nucleic acid molecules of the instant invention are not limiting within the general limits stated.

In one embodiment, the invention provides a method for producing a class of nucleic acid-based gene modulating agents, which exhibit a high degree of specificity for a viral reverse transcriptase such as HBV reverse transcriptase or reverse transcriptase primer such as a HBV reverse transcriptase primer. For example, the nucleic acid molecule is preferably targeted to a highly conserved nucleic acid binding region of the viral reverse transcriptase such that specific treatment of a disease or condition can be provided with either one or several nucleic acid molecules of the invention. Such nucleic acid molecules can be delivered exogenously to specific tissue or cellular targets as required. Alternatively, the nucleic acid molecules can be expressed from DNA and/or RNA vectors that are delivered to specific cells.

In another embodiment, the invention provides a method for producing a class of nucleic acid-based gene modulating agents which exhibit a high degree of specificity for a viral enhancer regions such as the HBV Enhancer I core sequence. For example, the nucleic acid molecule is preferably targeted to a highly conserved transcription factor-binding region of the viral Enhancer I sequence such that specific treatment of a disease or condition can be provided with either one or several nucleic acid molecules of the invention. Such nucleic acid molecules can be delivered exogenously to specific tissue or cellular targets as required. Alternatively, the nucleic acid molecules can be expressed from DNA and/or RNA vectors that are delivered to specific cells.

In a another embodiment the invention provides a method for producing a class of enzymatic cleaving agents which exhibit a high degree of specificity for the RNA of a desired target. The enzymatic nucleic acid molecule, nuclease activating compound or chimera is preferably targeted to a highly conserved sequence region of a target mRNAs encoding HCV or HBV proteins such that specific treatment of a disease or condition can be provided with either one or several enzymatic nucleic acids. Such nucleic acid molecules can be delivered exogenously to specific cells as required. Alternatively, the enzymatic nucleic acid molecules can be expressed from DNA/RNA vectors that are delivered to specific cells. DNazymes can be synthesized chemically or expressed endogenously *in vivo*, by means of a single stranded DNA vector or equivalent thereof.

In another embodiment, the nucleic acid molecule of the invention binds irreversibly to the HBV reverse transcriptase target, for example by covalent attachment of the nucleic acid molecule to the reverse transcriptase primer sequence. The covalent attachment can be accomplished by introducing chemical modifications into the nucleic acid molecule's (for example, decoy or aptamer) sequence that are capable of forming covalent bonds to the reverse transcriptase primer sequence.

In another embodiment, the nucleic acid molecule of the invention binds irreversibly to the HBV Enhancer I sequence target, for example, by covalent attachment of the nucleic acid molecule to the HBV Enhancer I sequence. The covalent attachment can be accomplished by introducing chemical modifications into the nucleic acid molecule's sequence that are capable of forming covalent bonds to the reverse transcriptase primer sequence.

In another embodiment, the type I interferon contemplated by the invention is interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, polyethylene glycol consensus interferon.

In one embodiment, the invention features a composition comprising type I interferon and a nucleic acid molecule of the invention and a pharmaceutically acceptable carrier.

In another embodiment, the invention features a method of administering to a cell, for example a mammalian cell or human cell, a nucleic acid molecule of the invention independently or in conjunction with other therapeutic compounds, such as type I interferon or 3TC® (lamivudine), comprising contacting the cell with the nucleic acid molecule under conditions suitable for the administration.

In yet another embodiment, the invention features a method of administering to a cell, for example a mammalian cell or human cell, a nucleic acid molecule of the invention independently or in conjunction with other therapeutic compounds such as enzymatic nucleic acid molecules, antisense molecules, triplex forming oligonucleotides, 2,5-A chimeras, and/or RNAi, comprising contacting the cell with the nucleic acid molecule of the invention under conditions suitable for the administration.

In another embodiment, administration of a nucleic acid molecule of the invention is administered to a cell or patient in the presence of a delivery reagent, for example a lipid, cationic lipid, phospholipid, or liposome.

In one embodiment, the invention features novel nucleic acid-based techniques such as nucleic acid decoy molecules and/or aptamers, used alone or in combination with enzymatic nucleic acid molecules, antisense molecules, and/or RNAi, and methods for use to down regulate or modulate the expression of HBV RNA and/or replication of HBV.

In another embodiment, the invention features the use of one or more of the nucleic acid-based techniques to modulate the expression of the genes encoding HBV viral proteins. Specifically, the invention features the use of nucleic acid-based techniques to specifically modulate the expression of the HBV viral genome.

In another embodiment, the invention features the use of one or more of the nucleic acid-based techniques to modulate the activity, expression, or level of cellular proteins required for HBV replication. For example, the invention features the use of nucleic acid-based techniques to specifically modulate the activity of cellular proteins required for HBV replication.

In another embodiment, the invention features nucleic acid-based modulators (*e.g.*, nucleic acid decoy molecules, aptamers, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, triplex DNA, antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or modulate reverse transcriptase activity and/or the expression of RNA (*e.g.*, HBV) capable of progression and/or maintenance of HBV infection, hepatocellular carcinoma, liver disease and failure.

In another embodiment, the invention features nucleic acid-based techniques (*e.g.*, nucleic acid decoy molecules, aptamers, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acid molecules, triplex DNA, antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or modulate reverse transcriptase activity and/or the expression of HBV RNA.

In another embodiment, the invention features nucleic acid-based modulators (*e.g.*, nucleic acid decoy molecules, aptamers, enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, triplex DNA, siRNA, dsRNA, antisense nucleic acids containing RNA cleaving chemical groups) and methods for their use to down regulate or modulate Enhancer I mediated transcription activity and/or the expression of DNA (*e.g.*, HBV) capable of progression and/or maintenance of HBV infection, hepatocellular carcinoma, liver disease and failure.

In another embodiment, the invention features nucleic acid-based techniques (*e.g.*, nucleic acid decoy molecules, aptamers, enzymatic nucleic acid molecules, antisense nucleic acid molecules, triplex DNA, siRNA, antisense nucleic acids containing DNA cleaving chemical groups) and methods for their use to down regulate or modulate Enhancer I mediated transcription activity and/or the expression of HBV DNA.

In another embodiment, the invention features a nucleic acid sensor molecule having an enzymatic nucleic acid domain and a sensor domain that interacts with an HBV peptide, protein, or polynucleotide sequence, for example, HBV reverse transcriptase, HBV reverse transcriptase primer, or the Enhancer I element of the HBV pregenomic RNA, wherein such interaction results in modulation of the activity of the enzymatic nucleic acid domain of the nucleic acid sensor molecule. In another embodiment, the invention features HBV-specific nucleic acid sensor molecules or allozymes, and methods for their use to down regulate or

modulate the expression of HBV RNA capable of progression and/or maintenance of hepatitis, hepatocellular carcinoma, cirrhosis, and/or liver failure. In yet another embodiment, the enzymatic nucleic acid domain of a nucleic acid sensor molecule of the invention is a Hammerhead, Inozyme, G-cleaver, DNAzyme, Zinzyme, Amberzyme, or
 5 Hairpin enzymatic nucleic acid molecule.

In one embodiment, nucleic acid molecules of the invention are used to treat HBV-infected cells or a HBV-infected patient wherein the HBV is resistant or the patient does not respond to treatment with 3TC® (Lamivudine), either alone or in combination with other therapies under conditions suitable for the treatment.

10 In another embodiment, nucleic acid molecules of the invention are used to treat HBV-infected cells or a HBV-infected patient, wherein the HBV is resistant or the patient does not respond to treatment with Interferon, for example Infergen®, either alone or in combination with other therapies under conditions suitable for the treatment.

The invention also relates to *in vitro* and *in vivo* systems, including, e.g., mammalian
 15 systems for screening inhibitors of HBV. In one embodiment, the invention features a mouse, for example a male or female mouse, implanted with HepG2.2.15 cells, wherein the mouse is susceptible to HBV infection and capable of sustaining HBV DNA expression. One embodiment of the invention provides a mouse implanted with HepG2.2.15 cells, wherein said mouse sustains the propagation of HEPG2.2.15 cells and HBV production.

20 In another embodiment, a mouse of the invention has been infected with HBV for at least one week to at least eight weeks, including, for example at least 4 weeks.

In yet another embodiment, a mouse of the invention, for example a male or female mouse, is an immunocompromised mouse, for example a nu/nu mouse or a scid/scid mouse.

In one embodiment, the invention features a method of producing a mouse of the
 25 invention, comprising injecting, for example by subcutaneous injection, HepG2.2.15 (Sells, *et al.*, 1987, *Proc Natl Acad Sci U S A.*, 84, 1005-1009) cells into the mouse under conditions suitable for the propagation of HepG2.2.15 cells in said mouse. HepG2.2.15 cells can be suspended in, for example, Delbecco's PBS solution including calcium and magnesium. In another embodiment, HepG2.2.15 cells are selected for antibiotic resistance and are then
 30 introduced into the mouse under conditions suitable for the propagation of HepG2.2.15 cells in said mouse. A non-limiting example of antibiotic resistant HepG2.2.15 cells include G418 antibiotic resistant HepG2.2.15 cells.

In another embodiment, the invention features a method of screening a compound for therapeutic activity against HBV, comprising administering the compound to a mouse of the

invention and monitoring the the levels of HBV produced (e.g. by assaying for HBV DNA levels) in the mouse.

In one embodiment, a therapeutic compound or therapy contemplated by the invention is a lipid, steroid, peptide, protein, antibody, monoclonal antibody, humanized monoclonal
5 antibody, small molecule, and/or isomers and analogs thereof, and/or a cell.

In one embodiment, a therapeutic compound or therapy contemplated by the invention is a nucleic acid molecule, for example a nucleic acid molecule, such as an enzymatic nucleic acid molecule, antisense nucleic acid molecule, allozyme, peptide nucleic acid, decoy, triplex oligonucleotide, dsRNA, ssRNA, RNAi, siRNA, aptamer, or 2,5-A chimera used alone or in
10 combination with another therapy, for example antiviral therapy. Antiviral therapy can be, for example, treatment with 3TC® (Lamivudine) or interferon. Interferon can include, for example, consensus interferon or type I interferon. Type I interferon can include interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, or polyethylene glycol
15 consensus interferon.

In one embodiment, the invention features a non-human mammal implanted with HepG2.2.15 cells, wherein the non-human mammal is susceptible to HBV infection and capable of sustaining HBV DNA expression in the implanted HepG2.2.15 cells.

In another embodiment, a non-human mammal of the invention, for example a male or
20 female non-human mammal, has been infected with HBV for at least one week to at least eight weeks, including for example at least four weeks.

In yet another embodiment, a non-human mammal of the invention is an immunocompromised mammal, for example a nu/nu mammal or a scid/scid mammal.

In one embodiment, the invention features a method of producing a non-human
25 mammal comprising HepG2.2.15 cells comprising injecting, for example by subcutaneous injection, HepG2.2.15 cells into the non-human mammal under conditions suitable for the propagation of HepG2.2.15 cells in said non-human mammal.

In another embodiment, the invention features a method of screening a compound for therapeutic activity against HBV comprising administering the compound to a non-human
30 mammal of the invention and monitoring the levels of HBV produced (e.g. by assaying for HBV DNA levels) in the non-human mammals.

In one embodiment, a therapeutic compound or therapy contemplated by the invention is a nucleic acid molecule, for example an enzymatic nucleic acid molecule, allozyme,

antisense nucleic acid molecule, decoy, triplex oligonucleotide, dsRNA, ssRNA, RNAi, siRNA, or 2,5-A chimera used alone or in combination with another therapy, for example antiviral therapy.

Methods and chimeric immunocompromised heterologous non-human mammalian hosts, particularly mouse hosts, are provided for the expression of hepatitis B virus ("HBV"). In one embodiment, the chimeric hosts have transplanted viable, HepG2.2.15 cells in an immunocompromised host.

The non-human mammals contemplated by the invention are immunocompromised in normally inheriting the desired immune incapacity, or the desired immune incapacity can be created. For example, hosts with severe combined immunodeficiency, known as scid/scid hosts, are available. Rodentia, particularly mice, and equine, particularly horses, are presently available as scid/scid hosts, for example scid/scid mice and scid/scid rats. The scid/scid hosts lack functioning lymphocyte types, particularly B-cells and some T-cell types. In the scid/scid mouse hosts, the genetic defect appears to be a non-functioning recombinase, as the germline DNA is not rearranged to produce functioning surface immunoglobulin and T-cell receptors.

Any immunodeficient non-human mammals, e.g. mouse, can be used to generate the animal models described herein. The term "immunodeficient," as used herein, refers to a genetic alteration that impairs the animal's ability to mount an effective immune response. In this regard, an "effective immune response" is one which is capable of destroying invading pathogens such as (but not limited to) viruses, bacteria, parasites, malignant cells, and/or a xenogeneic or allogeneic transplant. In one embodiment, the immunodeficient mouse is a severe immunodeficient (SCID) mouse, which lacks recombinase activity that is necessary for the generation of immunoglobulin and functional T cell antigen receptors, and thus does not produce functional B and T lymphocytes. In another embodiment, the immunodeficient mouse is a nude mouse, which contains a genetic defect that results in the absence of a functional thymus, leading to T-cell and B-cell deficiencies. However, mice containing other immunodeficiencies (such as rag-1 or rag-2 knockouts, as described in Chen *et al.*, 1994, *Curr. Opin. Immunol.*, 6, 313-319 and Guidas *et al.*, 1995, *J. Exp. Med.*, 181, 1187-1195, or beige-nude mice, which also lack natural killer cells, as described in Kollmann *et al.*, 1993, *J. Exp. Med.*, 177, 821-832) can also be employed.

The introduction of HepG2.2.15 cells occurs with a host at an age less than about 25% of its normal lifespan, usually to 20% of the normal lifespan with mice, and the age will generally be of an age of about 3 to 10 weeks, more usually from about 4 to 8 weeks. The mice can be of either sex, can be neutered, and can be otherwise normal, except for the

immunocompromised state, or they can have one or more mutations, which can be naturally occurring or as a result of mutagenesis.

In another embodiment, the mouse model described herein is used to evaluate the effectiveness of the therapeutic compounds and methods. The terms "therapeutic compounds", "therapeutic methods" and "therapy" as used herein, encompass exogenous factors, such as dietary or environmental conditions, as well as pharmaceutical compositions "drugs" and vaccines. In one embodiment, the therapeutic method is an immunotherapy, which can include the treatment of the HBV bearing animal with populations of HBV-reactive immune cells. The therapeutic method can also, or alternatively, be a gene therapy (i.e., a therapy that involves treatment of the HBV-bearing mouse with a cell population that has been manipulated to express one or more genes, the products of which can possess anti-viral activity), see for example The Development of Human Gene Therapy, Theodore Friedmann, Ed. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1999. Therapeutic compounds of the invention can comprise a drug or composition with pharmaceutical activity that can be used to treat illness or disease. A therapeutic method can comprise the use of a plurality of compounds in a mixture or a distinct entity. Examples of such compounds include nucleosides, nucleic acids, nucleic acid chimeras, RNA and DNA oligonucleotides, peptide nucleic acids, enzymatic nucleic acid molecules, antisense nucleic acid molecules, decoys, triplex oligonucleotides, ssDNA, dsRNA, ssRNA, siRNA, 2,5-A chimeras, lipids, steroids, peptides, proteins, antibodies, monoclonal antibodies (see for example Hall, 1995, Science, 270, 915-916), small molecules, and/or isomers and analogs thereof.

The methods of this invention can be used to treat human hepatitis B virus infections, which include productive virus infection, latent or persistent virus infection, and HBV-induced hepatocyte transformation. The utility can be extended to other species of HBV that infect non-human animals where such infections are of veterinary importance.

Preferred binding sites of the nucleic acid molecules of the invention include, but are not limited, to the primer binding site on HBV reverse transcriptase, the primer binding sequences of the HBV RNA, and/or the HBV Enhancer I region of HBV DNA.

This invention further relates to nucleic acid molecules that target RNA species of hepatitis C virus (HCV) and/or encoded by the HCV. In one embodiment, applicant describes enzymatic nucleic acid molecules that specifically cleave HCV RNA and the selection and function thereof. The invention further relates to compounds and chimeric molecules comprising nuclease activating activity. The invention also relates to compositions and methods for the cleavage of RNA using these nuclease activating compounds and chimeras. Nucleic acid molecules, nuclease activating compounds and

chimeras, and compositions and methods of the invention can be used to treat diseases associated with HCV infection.

Due to the high sequence variability of the HCV genome, selection of nucleic acid molecules and nuclease activating compounds and chimeras for broad therapeutic applications preferably involve the conserved regions of the HCV genome. Thus, in one embodiment the present invention describes nucleic acid molecules that cleave the conserved regions of the HCV genome. The invention further describes compounds and chimeric molecules that activate cellular nucleases that cleave HCV RNA, including conserved regions of the HCV genome. Examples of conserved regions of the HCV genome include but are not limited to the 5'-Non Coding Region (NCR), the 5'-end of the core protein coding region, and the 3'- NCR. HCV genomic RNA contains an internal ribosome entry site (IRES) in the 5'-NCR which mediates translation independently of a 5'-cap structure (Wang *et al.*, 1993, *J. Virol.*, 67, 3338-44). The full-length sequence of the HCV RNA genome is heterologous among clinically isolated subtypes, of which there are at least 15 (Simmonds, 1995, *Hepatology*, 21, 570-583), however, the 5'-NCR sequence of HCV is highly conserved across all known subtypes, most likely to preserve the shared IRES mechanism (Okamoto *et al.*, 1991, *J. General Virol.*, 72, 2697-2704). In general, enzymatic nucleic acid molecules and nuclease activating compounds, and chimeras that cleave sites located in the 5' end of the HCV genome are expected to block translation while nucleic acid molecules and nuclease activating compounds, and chimeras that cleave sites located in the 3' end of the genome are expected to block RNA replication. Therefore, one nucleic acid molecule, compound, or chimera can be designed to cleave all the different isolates of HCV. Enzymatic nucleic acid molecules and nuclease activating compounds, and chimeras designed against conserved regions of various HCV isolates enable efficient inhibition of HCV replication in diverse patient populations and ensure the effectiveness of the nucleic acid molecules and nuclease activating compounds, and chimeras against HCV quasi species which evolve due to mutations in the non-conserved regions of the HCV genome.

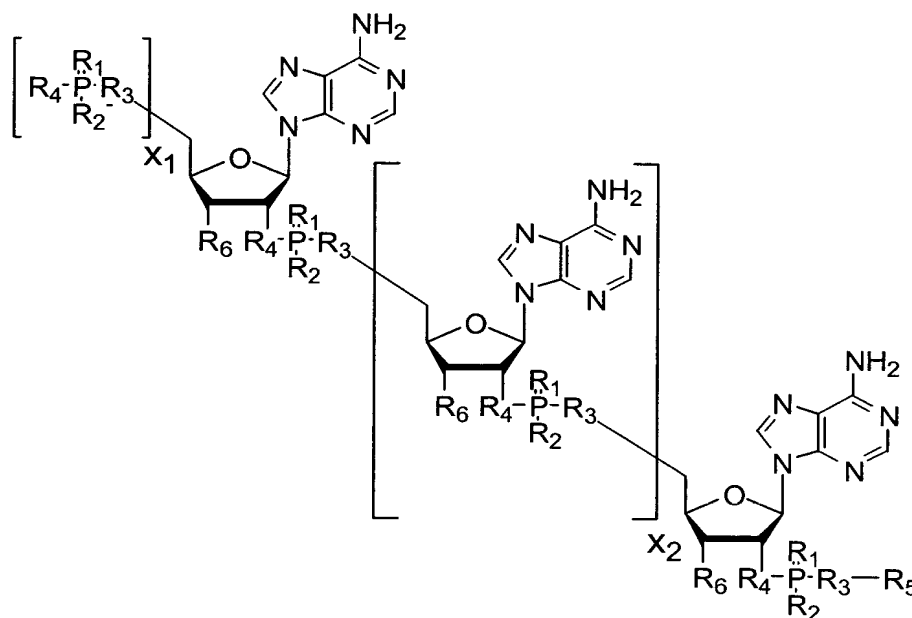
In one embodiment, the invention features an enzymatic nucleic acid molecule, preferably in the hammerhead, NCH (Inozyme), G-cleaver, amberzyme, zinzyme and/or DNAzyme motif, and the use thereof to down-regulate or inhibit the expression of HCV RNA.

In another embodiment, the invention features an enzymatic nucleic acid molecule, preferably in the hammerhead, Inozyme, G-cleaver, amberzyme, zinzyme and/or DNAzyme motif, and the use thereof to down-regulate or inhibit the expression of HCV minus strand RNA.

In yet another embodiment, the invention features a nuclease activating compound and/or a chimera and the use thereof to down-regulate or inhibit the expression of HCV RNA.

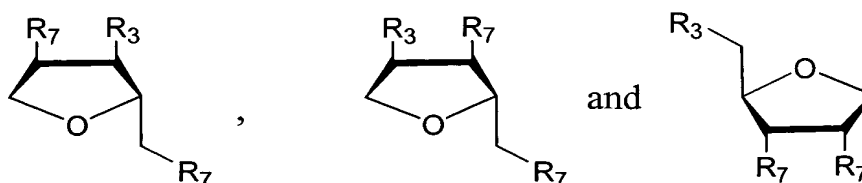
In another embodiment, the invention features the use of a nuclease activating compound and/or a chimera to inhibit the expression of HCVminus strand RNA.

5 In one embodiment, the invention features a compound having formula I:



10 wherein X_1 is an integer selected from the group consisting of 1, 2, and 3; X_2 is an integer greater than or equal to 1; R_6 is independently selected from the group including H, OH, NH_2 , O NH_2 , alkyl, S-alkyl, O-alkyl, O-alkyl-S-alkyl, O-alkoxyalkyl, allyl, O-allyl, and fluoro; each R_1 and R_2 are independently selected from the group consisting of O and S; each R_3 and R_4 are independently selected from the group consisting of O, N, and S; and R_5 is selected from the group consisting of alkyl, alkylamine, an oligonucleotide having any of SEQ ID NOS. 11343-16182, an oligonucleotide having a sequence complementary to a sequence selected from the group including SEQ ID NOS. 2594-7433, and abasic moiety.

15 In another embodiment, the abasic moiety of the instant invention is selected from the group consisting of:



wherein R_3 is selected from the group consisting of O, N, and S, and R_7 is independently selected from the group consisting of H, OH, NH₂, O-NH₂, alkyl, S-alkyl, O-alkyl, O-alkyl-S-alkyl, O-alkoxyalkyl, allyl, O-allyl, fluoro, oligonucleotide, alkyl, alkylamine and abasic moiety.

5 In another embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an enzymatic nucleic acid molecule.

10 In yet another embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an antisense nucleic acid molecule.

In another embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an enzymatic nucleic acid molecule selected from the group consisting of Hammerhead, Inozyme, G-cleaver, DNAzyme, Amberzyme, and Zinzyme motifs.

15 In another embodiment, the Inozyme enzymatic nucleic acid molecule of the instant invention comprises a stem II region of length greater than or equal to 2 base pairs.

20 In one embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an enzymatic nucleic acid comprising between 12 and 100 bases complementary to an RNA derived from HCV.

In another embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an enzymatic nucleic acid comprising between 14 and 24 bases complementary to said RNA derived from HCV.

25 In one embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an antisense nucleic acid comprising between 12 and 100 bases complementary to an RNA derived from HCV.

30 In another embodiment, the oligonucleotide R_5 of Formula I having a sequence complementary to a sequence selected from the group consisting of SEQ ID NOS. 2594-7433 is an antisense nucleic acid comprising between 14 and 24 bases complementary to said RNA derived from HCV.

In another embodiment, the invention features a composition comprising a compound of Formula I, in a pharmaceutically acceptable carrier.

In yet another embodiment, the invention features a mammalian cell comprising a compound of Formula I. For example, the mammalian cell comprising a compound of
5 Formula I can be a human cell.

In one embodiment, the invention features a method for the treatment of cirrhosis, liver failure, hepatocellular carcinoma, or a condition associated with HCV infection comprising the step of administering to a patient a compound of Formula I under conditions suitable for said treatment.

10 In another embodiment, the invention features a method of treatment of a patient having a condition associated with HCV infection comprising contacting cells of said patient with a compound having Formula I, and further comprising the use of one or more drug therapies under conditions suitable for said treatment. For example, the other therapies of the
15 instant invention can be selected from the group consisting of type I interferon, interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, polyethylene glycol consensus interferon, treatment with an enzymatic nucleic acid molecule, and treatment with an antisense molecule.

20 In another embodiment, the other therapies of the instant invention, for example type I interferon, interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, polyethylene glycol consensus interferon, treatment with an enzymatic nucleic acid molecule, and treatment with an antisense nucleic acid molecule, and the compound having Formula I are administered separately in separate pharmaceutically acceptable carriers.

25 In yet another embodiment, the other therapies of the instant invention, for example type I interferon, interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon alpha 2b, polyethylene glycol consensus interferon, treatment with an enzymatic nucleic acid molecule, and treatment with an antisense nucleic acid molecule, and the compound having Formula I
30 are administered simultaneously in a pharmaceutically acceptable carrier. The invention features a composition comprising a compound of Formula I and one or more of the above-listed compounds in a pharmaceutically acceptable carrier.

In yet another embodiment, the invention features a method for inhibiting HCV replication in a mammalian cell comprising the step of administering to said cell a compound having Formula I under conditions suitable for said inhibition.

5 In another embodiment, the invention features a method of cleaving a separate RNA molecule (i.e., HCV RNA or RNA necessary for HCV replication) comprising contacting a compound having Formula I with the separate RNA molecule under conditions suitable for the cleavage of the separate RNA molecule. In one example, the method of cleaving a separate RNA molecule is carried out in the presence of a divalent cation, for example Mg²⁺.

10 In yet another embodiment, the method of cleaving a separate RNA molecule of the invention is carried out in the presence of a protein nuclease, for example RNase L.

In one embodiment, a compound having Formula I is chemically synthesized. In one embodiment, a compound having Formula I comprises at least one 2'-sugar modification, at least one nucleic acid base modification, and/or at least one phosphate modification.

15 The nucleic acid-based modulators of the invention are added directly, or can be complexed with cationic lipids, packaged within liposomes, or otherwise delivered to target cells or tissues. The nucleic acid or nucleic acid complexes can be locally administered to relevant tissues *ex vivo*, or *in vivo* through injection, infusion pump or stent, with or without their incorporation in biopolymers. In particular embodiments, the nucleic acid molecules of the invention comprise sequences shown in **Tables IV-XI, XIV-XV and XVIII-XXIII**.
20 Examples of such nucleic acid molecules consist essentially of sequences defined in the tables.

The nucleic acid-based inhibitors, nuclease activating compounds and chimeras of the invention are added directly, or can be complexed with cationic lipids, packaged within liposomes, or otherwise delivered to target cells or tissues. The nucleic acid or nucleic acid
25 complexes, and nuclease activating compounds or chimeras can be locally administered to relevant tissues *ex vivo*, or *in vivo* through injection or infusion pump, with or without their incorporation in biopolymers. In preferred embodiments, the enzymatic nucleic acid inhibitors, and nuclease activating compounds or chimeras comprise sequences, which are complementary to the substrate sequences in **Tables XVIII, XIX, XX and XXIII**. Examples
30 of such enzymatic nucleic acid molecules also are shown in **Tables XVIII, XIX, XX, XXI and XXIII**. Examples of such enzymatic nucleic acid molecules consist essentially of sequences defined in these tables. In additional embodiments, the enzymatic nucleic acid inhibitors of the invention that comprise sequences which are complementary to the substrate sequences in **Tables XVIII, XIX, XX and XXIII** are covalently attached to nuclease

activating compound or chimeras of the invention, for example a compound having Formula I.

In yet another embodiment, the invention features antisense nucleic acid molecules and 2-5A chimera including sequences complementary to the substrate sequences shown in
5 **Tables XVIII, XIX, XX and XXIII**. Such nucleic acid molecules can include sequences as shown for the binding arms of the enzymatic nucleic acid molecules in **Tables XVIII, XIX, XX, XXI and XXIII**. Similarly, triplex molecules can be provided targeted to the corresponding DNA target regions, and containing the DNA equivalent of a target sequence or a sequence complementary to the specified target (substrate) sequence. Typically,
10 antisense molecules are complementary to a target sequence along a single contiguous sequence of the antisense molecule. However, in certain embodiments, an antisense molecule can bind to substrate such that the substrate molecule forms a loop, and/or an antisense molecule can bind such that the antisense molecule forms a loop. Thus, the antisense molecule can be complementary to two (or even more) non-contiguous substrate
15 sequences or two (or even more) non-contiguous sequence portions of an antisense molecule can be complementary to a target sequence or both.

In one embodiment, the invention features nucleic acid molecules and nuclease activating compounds or chimeras that inhibit gene expression and/or viral replication. These chemically or enzymatically synthesized nucleic acid molecules can contain substrate binding
20 domains that bind to accessible regions of their target mRNAs. The nucleic acid molecules also contain domains that catalyze the cleavage of RNA. The enzymatic nucleic acid molecules are preferably molecules of the hammerhead, Inozyme, DNAzyme, Zinzyme, Amberzyme, and/or G-cleaver motifs. Upon binding, the enzymatic nucleic acid molecules cleave the target mRNAs, preventing translation and protein accumulation. In the absence of
25 the expression of the target gene, HCV gene expression and/or replication is inhibited.

In another aspect, the invention provides mammalian cells containing one or more nucleic acid molecules and/or expression vectors of this invention. The one or more nucleic acid molecules can independently be targeted to the same or different sites.

In one embodiment, nucleic acid decoys, aptamers, siRNA, enzymatic nucleic acids or
30 antisense molecules that interact with target protein and/or RNA molecules and modulate HBV (specifically HBV reverse transcriptase, or transcription of HBV genomic DNA) activity are expressed from transcription units inserted into DNA or RNA vectors. The recombinant vectors are preferably DNA plasmids or viral vectors. Decoys, aptamers, enzymatic nucleic acid or antisense expressing viral vectors can be constructed based on, but
35 not limited to, adeno-associated virus, retrovirus, adenovirus, or alphavirus. Preferably, the recombinant vectors capable of expressing the decoys, aptamers, enzymatic nucleic acids or

antisense are delivered as described above, and persist in target cells. Alternatively, viral vectors can be used that provide for transient expression of decoys, aptamers, siRNA, enzymatic nucleic acids or antisense. Such vectors can be repeatedly administered as necessary. Once expressed, the decoys, aptamers, enzymatic nucleic acids or antisense bind to the target protein and/or RNA and modulate its function or expression. Delivery of decoy, aptamer, siRNA, enzymatic nucleic acid or antisense expressing vectors can be systemic, such as by intravenous or intramuscular administration, by administration to target cells explanted from the patient followed by reintroduction into the patient, or by any other means that would allow for introduction into the desired target cell. DNA based nucleic acid molecules of the invention can be expressed via the use of a single stranded DNA intracellular expression vector.

In one embodiment, nucleic acid molecules and nuclease activating compounds or chimeras are added directly, or can be complexed with cationic lipids, packaged within liposomes, or otherwise delivered to target cells. The nucleic acid or nucleic acid complexes can be locally administered to relevant tissues *ex vivo*, or *in vivo* through injection, infusion pump or stent, with or without their incorporation in biopolymers. In another preferred embodiment, the nucleic acid molecule, nuclease activating compound or chimera is administered to the site of HBV or HCV activity (e.g., hepatocytes) in an appropriate liposomal vehicle.

In another embodiment, nucleic acid molecules that cleave target molecules and inhibit HCV activity are expressed from transcription units inserted into DNA or RNA vectors. The recombinant vectors are preferably DNA plasmids or viral vectors. Nucleic acid molecule expressing viral vectors can be constructed based on, but not limited to, adeno-associated virus, retrovirus, adenovirus, or alphavirus. Preferably, the recombinant vectors capable of expressing the nucleic acid molecules are delivered as described above, and persist in target cells. Alternatively, viral vectors can be used that provide for transient expression of nucleic acid molecules. Such vectors can be repeatedly administered as necessary. Once expressed, the nucleic acid molecules cleave the target mRNA. Delivery of enzymatic nucleic acid molecule expressing vectors can be systemic, such as by intravenous or intramuscular administration, by administration to target cells explanted from the patient followed by reintroduction into the patient, or by any other means that would allow for introduction into the desired target cell (for a review see Couture and Stinchcomb, 1996, *TIG.*, 12, 510). In another aspect of the invention, nucleic acid molecules that cleave target molecules and inhibit viral replication are expressed from transcription units inserted into DNA, RNA, or viral vectors. Preferably, the recombinant vectors capable of expressing the nucleic acid molecules are locally delivered as described above, and transiently persist in smooth muscle

cells. However, other mammalian cell vectors that direct the expression of RNA can be used for this purpose.

The nucleic acid molecules of the instant invention, individually, or in combination or in conjunction with other drugs, and/or therapies can be used to treat diseases or conditions discussed herein. For example, to treat a disease or condition associated with the levels of HBV or HCV, the nucleic acid molecules can be administered to a patient or can be administered to other appropriate cells evident to those skilled in the art, individually or in combination with one or more drugs under conditions suitable for the treatment.

In a further embodiment, the described molecules, such as decoys, aptamers, antisense, enzymatic nucleic acids, or nuclease activating compounds and chimeras can be used in combination with other known treatments to treat conditions or diseases discussed above. For example, the described molecules could be used in combination with one or more known therapeutic agents to treat HBV infection, HCV infection, hepatitis, hepatocellular carcinoma, cancer, cirrhosis, and liver failure. Such therapeutic agents can include, but are not limited to, nucleoside analogs selected from the group comprising Lamivudine (3TC®), L-FMAU, and/or adefovir dipivoxil (for a review of applicable nucleoside analogs, see Colacino and Staschke, 1998, *Progress in Drug Research*, 50, 259-322). Immunomodulators selected from the group comprising Type 1 Interferon, therapeutic vaccines, steroids, and 2'-5' oligoadenylates (for a review of 2'-5' Oligoadenylates, see Charubala and Pfeleiderer, 1994, *Progress in Molecular and Subcellular Biology*, 14, 113-138).

Nucleic acid molecules, nuclease activating compounds and chimeras of the invention, individually, or in combination or in conjunction with other drugs, can be used to treat diseases or conditions discussed above. For example, to treat a disease or condition associated with HBV or HCV levels, the patient can be treated, or other appropriate cells can be treated, as is evident to those skilled in the art.

In a further embodiment, the described molecules can be used in combination with other known treatments to treat conditions or diseases discussed above. For example, the described molecules can be used in combination with one or more known therapeutic agents to treat liver failure, hepatocellular carcinoma, cirrhosis, and/or other disease states associated with HBV or HCV infection. Additional known therapeutic agents are those comprising antivirals, interferons, and/or antisense compounds.

The term "inhibit" or "down-regulate" as used herein refers to the expression of the gene, or level of RNAs or equivalent RNAs encoding one or more protein subunits or components, or activity of one or more protein subunits or components, such as HBV protein or proteins, is reduced below that observed in the absence of the therapies of the invention.

In one embodiment, inhibition or down-regulation with enzymatic nucleic acid molecule preferably is below that level observed in the presence of an enzymatically inactive or attenuated molecule that is able to bind to the same site on the target RNA, but is unable to cleave that RNA. In another embodiment, inhibition or down-regulation with antisense oligonucleotides is preferably below that level observed in the presence of, for example, an oligonucleotide with scrambled sequence or with mismatches. In another embodiment, inhibition or down-regulation of HBV with the nucleic acid molecule of the instant invention is greater in the presence of the nucleic acid molecule than in its absence.

The term "up-regulate" as used herein refers to the expression of the gene, or level of RNAs or equivalent RNAs encoding one or more protein subunits or components, or activity of one or more protein subunits or components, such as HBV or HCV protein or proteins, is greater than that observed in the absence of the therapies of the invention. For example, the expression of a gene, such as HBV or HCV genes, can be increased in order to treat, prevent, ameliorate, or modulate a pathological condition caused or exacerbated by an absence or low level of gene expression.

The term "modulate" as used herein refers to the expression of the gene, or level of RNAs or equivalent RNAs encoding one or more protein subunits or components, or activity of one or more proteins is up-regulated or down-regulated, such that the expression, level, or activity is greater than or less than that observed in the absence of the therapies of the invention.

The term "decoy " as used herein refers to a nucleic acid molecule, for example RNA or DNA, or aptamer that is designed to preferentially bind to a predetermined ligand. Such binding can result in the inhibition or activation of a target molecule. A decoy or aptamer can compete with a naturally occurring binding target for the binding of a specific ligand. For example, it has been shown that over-expression of HIV trans-activation response (TAR) RNA can act as a "decoy" and efficiently binds HIV tat protein, thereby preventing it from binding to TAR sequences encoded in the HIV RNA (Sullenger *et al.*, 1990, *Cell*, 63, 601-608). This is but a specific example and those in the art will recognize that other embodiments can be readily generated using techniques generally known in the art, see for example Gold *et al.*, 1995, *Annu. Rev. Biochem.*, 64, 763; Brody and Gold, 2000, *J. Biotechnol.*, 74, 5; Sun, 2000, *Curr. Opin. Mol. Ther.*, 2, 100; Kusser, 2000, *J. Biotechnol.*, 74, 27; Hermann and Patel, 2000, *Science*, 287, 820; and Jayasena, 1999, *Clinical Chemistry*, 45, 1628. Similarly, a decoy can be designed to bind to HBV or HCV proteins and block the binding of HBV or HCV DNA or RNA or a decoy can be designed to bind to HBV or HCV proteins and prevent molecular interaction with the HBV or HCV proteins.

By "aptamer" or "nucleic acid aptamer" as used herein is meant a nucleic acid molecule that binds specifically to a target molecule wherein the nucleic acid molecule has sequence that is distinct from sequence recognized by the target molecule in its natural setting. Alternately, an aptamer can be a nucleic acid molecule that binds to a target molecule where the target molecule does not naturally bind to a nucleic acid. The target molecule can be any molecule of interest. For example, the aptamer can be used to bind to a ligand-binding domain of a protein, thereby preventing interaction of the naturally occurring ligand with the protein. This is a non-limiting example and those in the art will recognize that other embodiments can be readily generated using techniques generally known in the art, see for example Gold *et al.*, 1995, *Annu. Rev. Biochem.*, 64, 763; Brody and Gold, 2000, *J. Biotechnol.*, 74, 5; Sun, 2000, *Curr. Opin. Mol. Ther.*, 2, 100; Kusser, 2000, *J. Biotechnol.*, 74, 27; Hermann and Patel, 2000, *Science*, 287, 820; and Jayasena, 1999, *Clinical Chemistry*, 45, 1628.

By "enzymatic nucleic acid molecule" is meant a nucleic acid molecule that has complementarity in a substrate binding region to a specified gene target, and also has an enzymatic activity which is active to specifically cleave a target RNA molecule. That is, the enzymatic nucleic acid molecule is able to intermolecularly cleave a RNA molecule and thereby inactivate a target RNA molecule. These complementary regions allow sufficient hybridization of the enzymatic nucleic acid molecule to a target RNA molecule and thus permit cleavage. One hundred percent complementarity is preferred, but complementarity as low as 50-75% may also be useful in this invention (see for example Werner and Uhlenbeck, 1995, *Nucleic Acids Research*, 23, 2092-2096; Hammann *et al.*, 1999, *Antisense and Nucleic Acid Drug Dev.*, 9, 25-31). The nucleic acids can be modified at the base, sugar, and/or phosphate groups. The term enzymatic nucleic acid is used interchangeably with phrases such as ribozymes, catalytic RNA, enzymatic RNA, catalytic DNA, aptazyme or aptamer-binding ribozyme, regulatable ribozyme, catalytic oligonucleotides, nucleozyme, DNAzyme, RNA enzyme, endoribonuclease, endonuclease, minizyme, leadzyme, oligozyme or DNA enzyme. All of these terminologies describe nucleic acid molecules with enzymatic activity. The specific enzymatic nucleic acid molecules described in the instant application are not limiting in the invention and those skilled in the art will recognize that all that is important in an enzymatic nucleic acid molecule of this invention is that it have a specific substrate binding site which is complementary to one or more of the target nucleic acid regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart a nucleic acid cleaving activity to the molecule (Cech *et al.*, U.S. Patent No. 4,987,071; Cech *et al.*, 1988, *JAMA* 260:20 3030-4).

By "nucleic acid molecule" as used herein is meant a molecule comprising nucleotides. The nucleic acid can be single, double, or multiple stranded and can comprise modified or unmodified nucleotides or non-nucleotides or various mixtures and combinations thereof.

By "enzymatic portion" or "catalytic domain" is meant that portion/region of the enzymatic nucleic acid molecule essential for cleavage of a nucleic acid substrate (for example see **Figures 1-5**).

By "substrate binding arm" or "substrate binding domain" is meant that portion/region of a ribozyme which is complementary to (*i.e.*, able to base-pair with) a portion of its substrate. Generally, such complementarity is 100%, but can be less if desired. For example, as few as 10 bases out of 14 may be base-paired (see for example Werner and Uhlenbeck, 1995, *Nucleic Acids Research*, 23, 2092-2096; Hammann *et al.*, 1999, *Antisense and Nucleic Acid Drug Dev.*, 9, 25-31). Such arms are shown generally in **Figures 1-5**. That is, these arms contain sequences within a ribozyme which are intended to bring ribozyme and target RNA together through complementary base-pairing interactions. The ribozyme of the invention can have binding arms that are contiguous or non-contiguous and may be of varying lengths. The length of the binding arm(s) are preferably greater than or equal to four nucleotides and of sufficient length to stably interact with the target RNA; specifically 12-100 nucleotides; more specifically 14-24 nucleotides long (see for example Werner and Uhlenbeck, *supra*; Hamman *et al.*, *supra*; Hampel *et al.*, EP0360257; Berzal-Herrance *et al.*, 1993, *EMBO J.*, 12, 2567-73). If two binding arms are chosen, the design is such that the length of the binding arms are symmetrical (*i.e.*, each of the binding arms is of the same length; *e.g.*, five and five nucleotides, six and six nucleotides or seven and seven nucleotides long) or asymmetrical (*i.e.*, the binding arms are of different length; *e.g.*, six and three nucleotides; three and six nucleotides long; four and five nucleotides long; four and six nucleotides long; four and seven nucleotides long; and the like).

By "nuclease activating compound" is meant a compound, for example a compound having Formula I, that activates the cleavage of an RNA by a nuclease. The nuclease can comprise RNase L. By "nuclease activating chimera" or "chimera" is meant a nuclease activating compound, for example a compound having Formula I, that is attached to a nucleic acid molecule, for example a nucleic acid molecule that binds preferentially to a target RNA. These chimeric nucleic acid molecules can comprise a nuclease activating compound and an antisense nucleic acid molecule, for example a 2',5'-oligoadenylate antisense chimera, or an enzymatic nucleic acid molecule, for example a 2',5'-oligoadenylate enzymatic nucleic acid chimera.

By "Inozyme" or "NCH" motif or configuration is meant, an enzymatic nucleic acid molecule comprising a motif as is generally described as NCH Rz in Ludwig *et al.*,

International PCT Publication No. WO 98/58058 and US Patent Application Serial No. 08/878,640. Inozymes possess endonuclease activity to cleave RNA substrates having a cleavage triplet NCH/, where N is a nucleotide, C is cytidine and H is adenosine, uridine or cytidine, and / represents the cleavage site. Inozymes can also possess endonuclease activity to cleave RNA substrates having a cleavage triplet NCN/, where N is a nucleotide, C is cytidine, and / represents the cleavage site.

By “G-cleaver” motif or configuration is meant, an enzymatic nucleic acid molecule comprising a motif as is generally described in Eckstein *et al.*, US 6,127,173 and in Kore *et al.*, 1998, *Nucleic Acids Research* 26, 4116-4120. G-cleavers possess endonuclease activity to cleave RNA substrates having a cleavage triplet NYN/, where N is a nucleotide, Y is uridine or cytidine and / represents the cleavage site. G-cleavers can be chemically modified.

By “zinzyme” motif or configuration is meant, an enzymatic nucleic acid molecule comprising a motif as is generally described in Beigelman *et al.*, International PCT publication No. WO 99/55857 and US Patent Application Serial No. 09/918,728. Zinzymes possess endonuclease activity to cleave RNA substrates having a cleavage triplet including but not limited to, YG/Y, where Y is uridine or cytidine, and G is guanosine and / represents the cleavage site. Zinzymes can be chemically modified to increase nuclease stability through various substitutions, including substituting 2'-O-methyl guanosine nucleotides for guanosine nucleotides. In addition, differing nucleotide and/or non-nucleotide linkers can be used to substitute the 5'-gaaa-2' loop of the motif. Zinzymes represent a non-limiting example of an enzymatic nucleic acid molecule that does not require a ribonucleotide (2'-OH) group within its own nucleic acid sequence for activity.

By “amberzyme” motif or configuration is meant, an enzymatic nucleic acid molecule comprising a motif as is generally described in Beigelman *et al.*, International PCT publication No. WO 99/55857 and US Patent Application Serial No. 09/476,387. Amberzymes possess endonuclease activity to cleave RNA substrates having a cleavage triplet NG/N, where N is a nucleotide, G is guanosine, and / represents the cleavage site. Amberzymes can be chemically modified to increase nuclease stability. In addition, differing nucleoside and/or non-nucleoside linkers can be used to substitute the 5'-gaaa-3' loops of the motif. Amberzymes represent a non-limiting example of an enzymatic nucleic acid molecule that does not require a ribonucleotide (2'-OH) group within its own nucleic acid sequence for activity.

By ‘DNAzyme’ is meant, an enzymatic nucleic acid molecule that does not require the presence of a 2'-OH group within its own nucleic acid sequence for activity. In particular embodiments, the enzymatic nucleic acid molecule can have an attached linker or linkers or other attached or associated groups, moieties, or chains containing one or more nucleotides

with 2'-OH groups. DNAzymes can be synthesized chemically or expressed endogenously *in vivo*, by means of a single stranded DNA vector or equivalent thereof. Non-limiting examples of DNAzymes are generally reviewed in Usman *et al.*, US patent No., 6,159,714; Chartrand *et al.*, 1995, *NAR* 23, 4092; Breaker *et al.*, 1995, *Chem. Bio.* 2, 655; Santoro *et al.*, 1997, *PNAS* 94, 4262; Breaker, 1999, *Nature Biotechnology*, 17, 422-423; and Santoro *et al.*, 2000, *J. Am. Chem. Soc.*, 122, 2433-39. The "10-23" DNAzyme motif is one particular type of DNAzyme that was evolved using *in vitro* selection as generally described in Joyce *et al.*, US 5,807,718 and Santoro *et al.*, *supra*. Additional DNAzyme motifs can be selected for using techniques similar to those described in these references, and hence, are within the scope of the present invention.

By "nucleic acid sensor molecule" or "allozyme" as used herein is meant a nucleic acid molecule comprising an enzymatic domain and a sensor domain, where the enzymatic nucleic acid domain's ability to catalyze a chemical reaction is dependent on the interaction with a target signaling molecule, such as a nucleic acid, polynucleotide, oligonucleotide, peptide, polypeptide, or protein, for example HBV RT, HBV RT primer, or HBV Enhancer I sequence. The introduction of chemical modifications, additional functional groups, and/or linkers, to the nucleic acid sensor molecule can provide enhanced catalytic activity of the nucleic acid sensor molecule, increased binding affinity of the sensor domain to a target nucleic acid, and/or improved nuclease/chemical stability of the nucleic acid sensor molecule, and are hence within the scope of the present invention (see for example Usman *et al.*, US Patent Application No. 09/877,526, George *et al.*, US Patent Nos. 5,834,186 and 5,741,679, Shih *et al.*, US Patent No. 5,589,332, Nathan *et al.*, US Patent No 5,871,914, Nathan and Ellington, International PCT publication No. WO 00/24931, Breaker *et al.*, International PCT Publication Nos. WO 00/26226 and 98/27104, and Sullenger *et al.*, US Patent Application Serial No. 09/205,520).

By "sensor component" or "sensor domain" of the nucleic acid sensor molecule as used herein is meant, a nucleic acid sequence (e.g., RNA or DNA or analogs thereof) which interacts with a target signaling molecule, for example a nucleic acid sequence in one or more regions of a target nucleic acid molecule or more than one target nucleic acid molecule, and which interaction causes the enzymatic nucleic acid component of the nucleic acid sensor molecule to either catalyze a reaction or stop catalyzing a reaction. In the presence of target signaling molecule of the invention, such as HBV RT, HBV RT primer, or HBV Enhancer I sequence, the ability of the sensor component, for example, to modulate the catalytic activity of the nucleic acid sensor molecule, is altered or diminished in a manner that can be detected or measured. The sensor component can comprise recognition properties relating to chemical or physical signals capable of modulating the nucleic acid sensor molecule via chemical or physical changes to the structure of the nucleic acid sensor molecule. The sensor component

can be derived from a naturally occurring nucleic acid binding sequence, for example, RNAs that bind to other nucleic acid sequences *in vivo*. Alternately, the sensor component can be derived from a nucleic acid molecule (aptamer), which is evolved to bind to a nucleic acid sequence within a target nucleic acid molecule. The sensor component can be covalently
 5 linked to the nucleic acid sensor molecule, or can be non-covalently associated. A person skilled in the art will recognize that all that is required is that the sensor component is able to selectively modulate the activity of the nucleic acid sensor molecule to catalyze a reaction.

By "target molecule" or "target signaling molecule" is meant a molecule capable of interacting with a nucleic acid sensor molecule, specifically a sensor domain of a nucleic acid
 10 sensor molecule, in a manner that causes the nucleic acid sensor molecule to be active or inactive. The interaction of the signaling agent with a nucleic acid sensor molecule can result in modification of the enzymatic nucleic acid component of the nucleic acid sensor molecule via chemical, physical, topological, or conformational changes to the structure of the molecule, such that the activity of the enzymatic nucleic acid component of the nucleic acid
 15 sensor molecule is modulated, for example is activated or inactivated. Signaling agents can comprise target signaling molecules such as macromolecules, ligands, small molecules, metals and ions, nucleic acid molecules including but not limited to RNA and DNA or analogs thereof, proteins, peptides, antibodies, polysaccharides, lipids, sugars, microbial or cellular metabolites, pharmaceuticals, and organic and inorganic molecules in a purified or
 20 unpurified form, for example HBV RT or HBV RT primer.

By "sufficient length" is meant a nucleic acid molecule long enough to provide the intended function under the expected condition. For example, a nucleic acid molecule of the invention needs to be of "sufficient length" to provide stable binding to a target site under the expected binding conditions and environment. In another non-limiting example, for the
 25 binding arms of an enzymatic nucleic acid, "sufficient length" means that the binding arm sequence is long enough to provide stable binding to a target site under the expected reaction conditions and environment. The binding arms are not so long as to prevent useful turnover of the nucleic acid molecule. By "stably interact" is meant interaction of the oligonucleotides with target nucleic acid (*e.g.*, by forming hydrogen bonds with complementary nucleotides in
 30 the target under physiological conditions) that is sufficient for the intended purpose (*e.g.*, cleavage of target RNA by an enzyme).

By "equivalent" RNA to HBV or HCV is meant to include those naturally occurring RNA molecules having homology (partial or complete) to HBV or HCV proteins or encoding for proteins with similar function as HBV or HCV in various organisms, including human,
 35 rodent, primate, rabbit, pig, protozoans, fungi, plants, and other microorganisms and parasites. The equivalent RNA sequence also includes in addition to the coding region,

regions such as 5'-untranslated region, 3'-untranslated region, introns, intron-exon junction and the like.

5 The term "component" of HBV or HCV as used herein refers to a peptide or protein subunit expressed from a HBV or HCV gene.

By "homology" is meant the nucleotide sequence of two or more nucleic acid molecules is partially or completely identical.

By "antisense nucleic acid", it is meant a non-enzymatic nucleic acid molecule that binds to target RNA by means of RNA-RNA or RNA-DNA or RNA-PNA (protein nucleic acid; Egholm *et al.*, 1993 *Nature* 365, 566) interactions and alters the activity of the target RNA (for a review, see Stein and Cheng, 1993 *Science* 261, 1004 and Woolf *et al.*, US patent No. 5,849,902). Typically, antisense molecules are complementary to a target sequence along a single contiguous sequence of the antisense molecule. However, in certain embodiments, an antisense molecule can bind to substrate such that the substrate molecule forms a loop, and/or an antisense molecule can bind such that the antisense molecule forms a loop. Thus, the antisense molecule can be complementary to two or more non-contiguous substrate sequences or two or more non-contiguous sequence portions of an antisense molecule can be complementary to a target sequence, or both. For a review of current antisense strategies, see Schmajuk *et al.*, 1999, *J. Biol. Chem.*, 274, 21783-21789, Delihhas *et al.*, 1997, *Nature*, 15, 751-753, Stein *et al.*, 1997, *Antisense N. A. Drug Dev.*, 7, 151, Crooke, 2000, *Methods Enzymol.*, 313, 3-45; Crooke, 1998, *Biotech. Genet. Eng. Rev.*, 15, 121-157, Crooke, 1997, *Ad. Pharmacol.*, 40, 1-49. Antisense molecules of the instant invention can include 2-5A antisense chimera molecules. In addition, antisense DNA can be used to target RNA by means of DNA-RNA interactions, thereby activating RNase H, which digests the target RNA in the duplex. The antisense oligonucleotides can comprise one or more RNase H activating region that is capable of activating RNase H cleavage of a target RNA. Antisense DNA can be synthesized chemically or expressed via the use of a single stranded DNA expression vector or equivalent thereof.

By "RNase H activating region" is meant a region (generally greater than or equal to 4-25 nucleotides in length, preferably from 5-11 nucleotides in length) of a nucleic acid molecule capable of binding to a target RNA to form a non-covalent complex that is recognized by cellular RNase H enzyme (see for example Arrow *et al.*, US 5,849,902; Arrow *et al.*, US 5,989,912). The RNase H enzyme binds to the nucleic acid molecule-target RNA complex and cleaves the target RNA sequence. The RNase H activating region comprises, for example, phosphodiester, phosphorothioate (for example, at least four of the nucleotides

are phosphorothioate substitutions; more specifically, 4-11 of the nucleotides are phosphorothioate substitutions), phosphorodithioate, 5'-thiophosphate, or methylphosphonate backbone chemistry or a combination thereof. In addition to one or more backbone chemistries described above, the RNase H activating region can also comprise a variety of sugar chemistries. For example, the RNase H activating region can comprise deoxyribose, arabino, fluoroarabino or a combination thereof, nucleotide sugar chemistry. Those skilled in the art will recognize that the foregoing are non-limiting examples and that any combination of phosphate, sugar and base chemistry of a nucleic acid that supports the activity of RNase H enzyme is within the scope of the definition of the RNase H activating region and the instant invention.

By "2-5A antisense" or "2-5A antisense chimera" is meant an antisense oligonucleotide containing a 5'-phosphorylated 2'-5'-linked adenylyate residue. These chimeras bind to target RNA in a sequence-specific manner and activate a cellular 2-5A-dependent ribonuclease which, in turn, cleaves the target RNA (Torrence et al., 1993 *Proc. Natl. Acad. Sci. USA* 90, 1300; Silverman et al., 2000, *Methods Enzymol.*, 313, 522-533; Player and Torrence, 1998, *Pharmacol. Ther.*, 78, 55-113).

By "triplex nucleic acid" or "triplex oligonucleotide" it is meant a polynucleotide or oligonucleotide that can bind to a double-stranded DNA in a sequence-specific manner to form a triple-strand helix. Formation of such triple helix structure has been shown to modulate transcription of the targeted gene (Duval-Valentin *et al.*, 1992, *Proc. Natl. Acad. Sci. USA*, 89, 504). Triplex nucleic acid molecules of the invention also include steric blocker nucleic acid molecules that bind to the Enhancer I region of HBV DNA (plus strand and/or minus strand) and prevent translation of HBV genomic DNA.

The term "single stranded RNA" (ssRNA) as used herein refers to a naturally occurring or synthetic ribonucleic acid molecule comprising a linear single strand, for example a ssRNA can be a messenger RNA (mRNA), transfer RNA (tRNA), ribosomal RNA (rRNA) etc. of a gene.

The term "single stranded DNA" (ssDNA) as used herein refers to a naturally occurring or synthetic deoxyribonucleic acid molecule comprising a linear single strand, for example, a ssDNA can be a sense or antisense gene sequence or EST (Expressed Sequence Tag).

The term "allozyme" as used herein refers to an allosteric enzymatic nucleic acid molecule, see for example George *et al.*, US Patent Nos. 5,834,186 and 5,741,679, Shih *et al.*, US Patent No. 5,589,332, Nathan *et al.*, US Patent No 5,871,914, Nathan and Ellington, International PCT publication No. WO 00/24931, Breaker *et al.*, International PCT

Publication Nos. WO 00/26226 and 98/27104, and Sullenger *et al.*, International PCT publication No. WO 99/29842.

The term "2-5A chimera" as used herein refers to an oligonucleotide containing a 5'-phosphorylated 2'-5'-linked adenylate residue. These chimeras bind to target RNA in a sequence-specific manner and activate a cellular 2-5A-dependent ribonuclease which, in turn, cleaves the target RNA (Torrence *et al.*, 1993 *Proc. Natl. Acad. Sci. USA* 90, 1300; Silverman *et al.*, 2000, *Methods Enzymol.*, 313, 522-533; Player and Torrence, 1998, *Pharmacol. Ther.*, 78, 55-113).

The term "double stranded RNA" or "dsRNA" as used herein refers to a double stranded RNA molecule capable of RNA interference "RNAi", including short interfering RNA "siRNA" see for example Bass, 2001, *Nature*, 411, 428-429; Elbashir *et al.*, 2001, *Nature*, 411, 494-498; and Kreutzer *et al.*, International PCT Publication No. WO 00/44895; Zernicka-Goetz *et al.*, International PCT Publication No. WO 01/36646; Fire, International PCT Publication No. WO 99/32619; Plaetinck *et al.*, International PCT Publication No. WO 00/01846; Mello and Fire, International PCT Publication No. WO 01/29058; Deschamps-Depaillette, International PCT Publication No. WO 99/07409; and Li *et al.*, International PCT Publication No. WO 00/44914.

By "gene" it is meant, a nucleic acid that encodes an RNA, for example, nucleic acid sequences including, but not limited to, structural genes encoding a polypeptide.

By "complementarity" is meant that a nucleic acid can form hydrogen bond(s) with another nucleic acid sequence by either traditional Watson-Crick or other non-traditional types. In reference to the nucleic molecules of the present invention, the binding free energy for a nucleic acid molecule with its target or complementary sequence is sufficient to allow the relevant function of the nucleic acid to proceed, e.g., ribozyme cleavage, antisense or triple helix modulation. Determination of binding free energies for nucleic acid molecules is well known in the art (see, e.g., Turner *et al.*, 1987, *CSH Symp. Quant. Biol.* LII pp.123-133; Frier *et al.*, 1986, *Proc. Nat. Acad. Sci. USA* 83:9373-9377; Turner *et al.*, 1987, *J. Am. Chem. Soc.* 109:3783-3785). A percent complementarity indicates the percentage of contiguous residues in a nucleic acid molecule that can form hydrogen bonds (e.g., Watson-Crick base pairing) with a second nucleic acid sequence (e.g., 5, 6, 7, 8, 9, 10 out of 10 being 50%, 60%, 70%, 80%, 90%, and 100% complementary). "Perfectly complementary" means that all the contiguous residues of a nucleic acid sequence will hydrogen bond with the same number of contiguous residues in a second nucleic acid sequence.

As used herein "cell" is used in its usual biological sense, and does not refer to an entire multicellular organism, e.g., specifically does not refer to a human. The cell can be present in

an organism, e.g., birds, plants and mammals such as humans, cows, sheep, apes, monkeys, swine, dogs, and cats. The cell can be prokaryotic (e.g., bacterial cell) or eukaryotic (e.g., mammalian or plant cell).

By “HBV proteins” or “HCV proteins” is meant, a protein or a mutant protein
5 derivative thereof, comprising sequence expressed and/or encoded by the HBV genome.

By “highly conserved sequence region” is meant a nucleotide sequence of one or more regions in a target gene does not vary significantly from one generation to the other or from one biological system to the other.

By “highly conserved nucleic acid binding region” is meant an amino acid sequence of
10 one or more regions in a target protein that does not vary significantly from one generation to the other or from one biological system to the other.

By “related to the levels of HBV” is meant that the reduction of HBV expression (specifically HBV gene) RNA levels and thus reduction in the level of the respective protein will relieve, to some extent, the symptoms of the disease or condition.

By “related to the levels of HCV” is meant that the reduction of HCV expression
15 (specifically HCV gene) RNA levels and thus reduction in the level of the respective protein will relieve, to some extent, the symptoms of the disease or condition.

By “RNA” is meant a molecule comprising at least one ribonucleotide residue. By
“ribonucleotide” is meant a nucleotide with a hydroxyl group at the 2’ position of a β -D-ribo-
20 furanose moiety.

By “vector” is meant any nucleic acid- and/or viral-based technique used to express and/or deliver a desired nucleic acid.

By "patient" is meant an organism, which is a donor or recipient of explanted cells or the cells themselves. "Patient" also refers to an organism to which the nucleic acid molecules
25 of the invention can be administered. In one embodiment, a patient is a mammal or mammalian cells. In another embodiment, a patient is a human or human cells.

Other features and advantages of the invention will be apparent from the following description of the preferred embodiments thereof, and from the claims.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

First the drawings will be described briefly.

Drawings

Figure 1 shows the secondary structure model for seven different classes of enzymatic nucleic acid molecules. Arrow indicates the site of cleavage. ----- indicate the target sequence. Lines interspersed with dots are meant to indicate tertiary interactions. - is meant to indicate base-paired interaction. **Group I Intron:** P1-P9.0 represent various stem-loop structures (Cech *et al.*, 1994, *Nature Struc. Bio.*, 1, 273). **RNase P (M1RNA):** EGS represents external guide sequence (Forster *et al.*, 1990, *Science*, 249, 783; Pace *et al.*, 1990, *J. Biol. Chem.*, 265, 3587). **Group II Intron:** 5'SS means 5' splice site; 3'SS means 3'-splice site; IBS means intron binding site; EBS means exon binding site (Pyle *et al.*, 1994, *Biochemistry*, 33, 2716). **VS RNA:** I-VI are meant to indicate six stem-loop structures; shaded regions are meant to indicate tertiary interaction (Collins, International PCT Publication No. WO 96/19577). **HDV Ribozyme:** I-IV are meant to indicate four stem-loop structures (Been *et al.*, US Patent No. 5,625,047). **Hammerhead Ribozyme:** I-III are meant to indicate three stem-loop structures; stems I-III can be of any length and may be symmetrical or asymmetrical (Usman *et al.*, 1996, *Curr. Op. Struct. Bio.*, 1, 527). **Hairpin Ribozyme:** Helix 1, 4 and 5 can be of any length; Helix 2 is between 3 and 8 base-pairs long; Y is a pyrimidine; Helix 2 (H2) is provided with a least 4 base pairs (*i.e.*, n is 1, 2, 3 or 4) and helix 5 can be optionally provided of length 2 or more bases (preferably 3 - 20 bases, *i.e.*, m is from 1 - 20 or more). Helix 2 and helix 5 may be covalently linked by one or more bases (*i.e.*, r is ≥ 1 base). Helix 1, 4 or 5 may also be extended by 2 or more base pairs (*e.g.*, 4 - 20 base pairs) to stabilize the ribozyme structure, and preferably is a protein binding site. In each instance, each N and N' independently is any normal or modified base and each dash represents a potential base-pairing interaction. These nucleotides may be modified at the sugar, base or phosphate. Complete base-pairing is not required in the helices, but is preferred. Helix 1 and 4 can be of any size (*i.e.*, o and p is each independently from 0 to any number, *e.g.*, 20) as long as some base-pairing is maintained. Essential bases are shown as specific bases in the structure, but those in the art will recognize that one or more may be modified chemically (abasic, base, sugar and/or phosphate modifications) or replaced with another base without significant effect. Helix 4 can be formed from two separate molecules, *i.e.*, without a connecting loop. The connecting loop when present may be a ribonucleotide with or without modifications to its base, sugar or phosphate. "q" \geq is 2 bases. The connecting loop can also be replaced with a non-nucleotide linker molecule. H refers to bases A, U, or C. Y refers to pyrimidine bases. "_____" refers to a covalent bond. (Burke *et al.*, 1996, *Nucleic Acids & Mol. Biol.*, 10, 129; Chowrira *et al.*, US Patent No. 5,631,359).

Figure 2 shows examples of chemically stabilized ribozyme motifs. **HH Rz**, represents hammerhead ribozyme motif (Usman *et al.*, 1996, *Curr. Op. Struct. Bio.*, 1, 527); **NCH Rz** represents the NCH ribozyme motif (Ludwig & Sproat, International PCT Publication No. WO 98/58058); **G-Cleaver**, represents G-cleaver ribozyme motif (Kore *et al.*, 1998, *Nucleic Acids Research*, 26, 4116-4120). **N** or **n**, represent independently a nucleotide which may be same or different and have complementarity to each other; **rI**, represents ribo-Inosine nucleotide; arrow indicates the site of cleavage within the target. Position 4 of the HH Rz and the NCH Rz is shown as having 2'-C-allyl modification, but those skilled in the art will recognize that this position can be modified with other modifications well known in the art, so long as such modifications do not significantly inhibit the activity of the ribozyme.

Figure 3 shows an example of the Amberzyme ribozyme motif that is chemically stabilized (see, for example, Beigelman *et al.*, International PCT publication No. WO 99/55857; also referred to as Class I Motif). The Amberzyme motif is a class of enzymatic nucleic acid molecules that do not require the presence of a ribonucleotide (2'-OH) group for activity.

Figure 4 shows an example of the Zinzyme A ribozyme motif that is chemically stabilized (see, for example, International PCT publication No. WO 99/55857; also referred to as Class A Motif). The Zinzyme motif is a class of enzymatic nucleic acid molecules that do not require the presence of a ribonucleotide (2'-OH) group for activity.

Figure 5 shows an example of a DNAzyme motif described by Santoro *et al.*, 1997, *PNAS*, 94, 4262.

Figure 6 is a bar graph showing the percent change in serum HBV DNA levels following fourteen days of ribozyme treatment in HBV transgenic mice. Ribozymes targeting sites 273 (RPI.18341) and 1833 (RPI.18371) of HBV RNA administered via continuous s.c. infusion at 10, 30, and 100 mg/kg/day are compared to continuous s.c. infusion administration of scrambled attenuated core ribozyme and saline controls, and orally administered 3TC® (300 mg/kg/day) and saline controls.

Figure 7 is a bar graph showing the mean serum HBV DNA levels following fourteen days of ribozyme treatment in HBV transgenic mice. Ribozymes targeting sites 273 (RPI.18341) and 1833 (RPI.18371) of HBV RNA administered via continuous s.c. infusion at 10, 30, and 100 mg/kg/day are compared to continuous s.c. infusion administration of scrambled attenuated core ribozyme and saline controls, and orally administered 3TC® (300 mg/kg/day) and saline controls.

Figure 8 is a bar graph showing the decrease in serum HBV DNA (log) levels following fourteen days of ribozyme treatment in HBV transgenic mice. Ribozymes targeting sites 273 (RPI.18341) and 1833 (RPI.18371) of HBV RNA administered via continuous s.c. infusion at 10, 30, and 100 mg/kg/day are compared to continuous s.c. infusion administration of scrambled attenuated core ribozyme and saline controls, and orally administered 3TC® (300 mg/kg/day) and saline controls.

Figure 9 is a bar graph showing the decrease in HBV DNA in HepG2.2.15 cells after treatment with ribozymes targeting sites 273 (RPI.18341), 1833 (RPI.18371), 1874 (RPI.18372), and 1873 (RPI.18418) of HBV RNA as compared to a scrambled attenuated core ribozyme (RPI.20995).

Figure 10 is a bar graph showing reduction in HBsAg levels following treatment of HepG2 cells with anti-HBV arm, stem, and loop-variant ribozymes (RPI.18341, RPI.22644, RPI.22645, RPI.22646, RPI.22647, RPI.22648, RPI.22649, and RPI.22650) targeting site 273 of the HBV pregenomic RNA as compared to a scrambled attenuated core ribozyme (RPI.20599).

Figure 11 is a bar graph showing reduction in HBsAg levels following treatment of HepG2 cells with RPI 18341 alone or in combination with Infergen®. At either 500 or 1000 units of Infergen®, the addition of 200 nM of RPI.18341 results in a 75-77% increase in anti-HBV activity as judged by the level of HBsAg secreted from the treated Hep G2 cells. Conversely, the anti-HBV activity of RPI.18341 (at 200 nM) is increased 31-39% when used in combination of 500 or 1000 units of Infergen®.

Figure 12 is a bar graph showing reduction in HBsAg levels following treatment of HepG2 cells with RPI 18341 alone or in combination with Lamivudine. At 25 nM Lamivudine (3TC®), the addition of 100 nM of RPI.18341 results in a 48% increase in anti-HBV activity as judged by the level of HBsAg secreted from treated Hep G2 cells. Conversely, the anti-HBV activity of RPI.18341 (at 100 nM) is increased 31% when used in combination with 25 nM Lamivudine.

Figure 13 shows a scheme which outlines the steps involved in HBV reverse transcription. The HBV polymerase/reverse transcriptase binds to the 5'-stem-loop of the HBV pregenomic RNA and synthesizes a primer from the UUCA template. The reverse transcriptase and tetramer primer are translocated to the 3'-DR1 site. The RT primer binds to the UUCA sequence in the DR1 element and minus strand synthesis begins.

Figure 14 shows a non-limiting example of inhibition of HBV reverse transcription. A decoy molecule binds to the HBV RT primer, thereby preventing translocation of the RT to the 3'-DR1 site and preventing minus strand synthesis.

Figure 15 shows data of a HBV nucleic acid screen of 2'-O-allyl modified nucleic acid molecules. The levels of HbsAg were determined by ELISA. Inhibition of HBV is correlated to HBsAg antigen levels.

Figure 16 shows data of a HBV nucleic acid screen of 2'-O-methyl modified nucleic acid molecules. The levels of HbsAg were determined by ELISA. Inhibition of HBV is correlated to HBsAg antigen levels.

Figure 17 shows dose response data of 2'-O-methyl modified nucleic acid molecules targeting the HBV reverse transcriptase primer compared to levels of HBsAg.

Figure 18 shows data of nucleic acid screen of nucleic acid molecules (200 nM) targeting the HBV Enhancer I core region compared to levels of HBsAg.

Figure 19 shows data of nucleic acid screen of nucleic acid molecules (400 nM) targeting the HBV Enhancer I core region compared to levels of HBsAg.

Figure 20 shows dose response data of nucleic acid molecules targeting the HBV Enhancer I core region compared to levels of HBsAg.

Figure 21 shows a graph depicting HepG2.2.15 tumor growth in athymic nu/nu female mice as tumor volume (mm³) vs time (days).

Figure 22 shows a graph depicting HepG2.2.15 tumor growth in athymic nu/nu female mice as tumor volume (mm³) vs time (days). Inoculated HepG2.2.15 cells were selected for antibiotic resistance to G418 before introduction into the mouse.

Figure 23 is a schematic representation of the Dual Reporter System utilized to demonstrate enzymatic nucleic acid mediated reduction of luciferase activity in cell culture.

Figure 24 shows a schematic view of the secondary structure of the HCV 5'UTR (Brown *et al.*, 1992, *Nucleic Acids Res.*, 20, 5041-45; Honda *et al.*, 1999, *J. Virol.*, 73, 1165-74). Major structural domains are indicated in bold. Enzymatic nucleic acid cleavage sites are indicated by arrows. Solid arrows denote sites amenable to amino-modified enzymatic nucleic acid inhibition. Lead cleavage sites (195 and 330) are indicated with oversized solid arrows.

Figure 25 shows a non-limiting example of a nuclease resistant enzymatic nucleic acid molecule. Binding arms are indicated as stem I and stem III. Nucleotide modifications are indicated as follows: 2'-O-methyl nucleotides, lowercase; ribonucleotides, uppercase G, A; 2'-amino-uridine, u; inverted 3'-3' deoxyabasic, **B**. The positions of phosphorothioate linkages at the 5'-end of each enzymatic nucleic acid are indicated by subscript "s". *H* indicates A, C or U ribonucleotide, *N'* indicates A, C G or U ribonucleotide in substrate, *n* indicates base complementary to the *N'*. The U4 and U7 positions in the catalytic core are indicated.

Figure 26 is a set of bar graphs showing enzymatic nucleic acid mediated inhibition of HCV-luciferase expression in OST7 cells. OST7 cells were transfected with complexes containing reporter plasmids (2 µg/mL), enzymatic nucleic acids (100 nM) and lipid. The ratio of HCV-firefly luciferase luminescence/Renilla luciferase luminescence was determined for each enzymatic nucleic acid tested and was compared to treatment with the ICR, an irrelevant control enzymatic nucleic acid lacking specificity to the HCV 5'UTR (adjusted to 1). Results are reported as the mean of triplicate samples \pm SD. In **Figure 26A**, OST7 cells were treated with enzymatic nucleic acids (100 nM) targeting conserved sites (indicated by cleavage site) within the HCV 5'UTR. In **Figure 26B**, OST7 cells were treated with a subset of enzymatic nucleic acids to lead HCV sites (indicated by cleavage site) and corresponding attenuated core (AC) controls. Percent decrease in firefly/Renilla luciferase ratio after treatment with active enzymatic nucleic acids as compared to treatment with corresponding ACs is shown when the decrease is \geq 50% and statistically significant. Similar results were obtained with 50 nM enzymatic nucleic acid.

Figure 27 is a series of line graphs showing the dose-dependent inhibition of HCV/luciferase expression following enzymatic nucleic acid treatment. Active enzymatic nucleic acid was mixed with corresponding AC to maintain a 100 nM total oligonucleotide concentration and the same lipid charge ratio. The concentration of active enzymatic nucleic acid for each point is shown. **Figure 27A–E** shows enzymatic nucleic acids targeting sites 79, 81, 142, 195, or 330, respectively. Results are reported as the mean of triplicate samples \pm SD.

Figure 28 is a set of bar graphs showing reduction of HCV/luciferase RNA and inhibition of HCV-luciferase expression in OST7 cells. OST7 cells were transfected with complexes containing reporter plasmids (2 µg /ml), enzymatic nucleic acids, BACs or SACs (50 nM) and lipid. Results are reported as the mean of triplicate samples \pm SD. In **Figure 28A** the ratio of HCV-firefly luciferase RNA/Renilla luciferase RNA is shown for each enzymatic nucleic acid or control tested. As compared to paired BAC controls (adjusted to 1), luciferase RNA levels were reduced by 40% and 25% for the site 195 or 330 enzymatic nucleic acids, respectively. In **Figure 28B** the ratio of HCV-firefly luciferase

luminescence/Renilla luciferase luminescence is shown after treatment with site 195 or 330 enzymatic nucleic acids or paired controls. As compared to paired BAC controls (adjusted to 1), inhibition of protein expression was 70% and 40% for the site 195 or 330 enzymatic nucleic acids, respectively $P < 0.01$.

Figure 29 is a set a bar graphs showing interferon (IFN) alpha 2a and 2b dose response in combination with site 195 anti-HCV enzymatic nucleic acid treatment. **Figure 29A** shows data for IFN alfa 2a treatment. **Figure 29B** shows data for IFN alfa 2b treatment. Viral yield is reported from HeLa cells pretreated with IFN in units/ml (U/ml) as indicated for 4 h prior to infection and then treated with either 200 nM control (SAC) or site 195 anti-HCV enzymatic nucleic acid (195 RZ) for 24 h after infection. Cells were infected with a MOI = 0.1 for 30 min and collected at 24 h post infection. Error bars represent the S.D. of the mean of triplicate determinations.

Figure 30 is a line graph showing site 195 anti-HCV enzymatic nucleic acid dose response in combination with interferon (IFN) alpha 2a and 2b pretreatment. Viral yield is reported from HeLa cells pretreated for 4 h with or without IFN and treated with doses of site 195 anti-HCV enzymatic nucleic acid (195 RZ) as indicated for 24 h after infection. Anti-HCV enzymatic nucleic acid was mixed with control oligonucleotide (SAC) to maintain a constant 200 nM total dose of nucleic acid for delivery. Cells were infected with a MOI = 0.1 for 30 min and collected at 24 h post infection. Error bars represent the S.D. of the mean of triplicate determinations.

Figure 31 is a set of bar graphs showing data from consensus interferon (CIFN)/enzymatic nucleic acid combination treatment. **Figure 31A** shows CIFN dose response with site 195 anti-HCV enzymatic nucleic acid treatment. Viral yield is reported from cells pretreated with CIFN in units/ml (U/ml) as indicated and treated with either 200 nM control (SAC) or site 195 anti-HCV enzymatic nucleic acid (195 RZ). **Figure 31B** shows site 195 anti-HCV enzymatic nucleic acid dose response with CIFN pretreatment. Viral yield is reported from cells pretreated with or without CIFN and treated with concentrations of site 195 anti-HCV enzymatic nucleic acid (195 RZ) as indicated. Anti-HCV enzymatic nucleic acid was mixed with control oligonucleotide (SAC) to maintain a constant 200 nM total dose of nucleic acid for delivery. Cells were infected with a MOI = 0.1 for 30 min. and collected at 24 h post infection. Error bars represent the S.D. of the mean of triplicate determinations.

Figure 32 is a bar graph showing enzymatic nucleic acid activity and enhanced antiviral effect of an anti-HCV enzymatic nucleic acid targeting site 195 used in combination with consensus interferon (CIFN). Viral yield is reported from cells treated as indicated. BAC, cells were treated with 200 nM BAC (binding attenuated control) for 24 h after infection; CIFN+BAC, cells were treated with 12.5 U/ml CIFN for 4 h prior to infection and

with 200 nM BAC for 24 h after infection; 195 RZ, cells were treated with 200 nM site 195 anti-HCV enzymatic nucleic acid for 24 h after infection; CIFN + 195 RZ, cells were treated with 12.5 U/ml CIFN for 4 h prior to infection and with 200 nM site 195 anti-HCV enzymatic nucleic acid for 24 h after infection. Cells were infected with a MOI = 0.1 for 30 min. Error bars represent the S.D. of the mean of triplicate determinations.

Figure 33 is a bar graph showing inhibition of a HCV-PV chimera replication by treatment with zinzyme enzymatic nucleic acid molecules targeting different sites within the HCV 5'-UTR compared to a scrambled attenuated core control (SAC) zinzyme.

Figure 34 is a bar graph showing inhibition of a HCV-PV chimera replication by antisense nucleic acid molecules targeting conserved regions of the HCV 5'-UTR compared to scrambled antisense controls.

Figure 35 shows the structure of compounds (2-5A) utilized in the study. "X" denotes the position of oxygen (O) in analog I or sulfur (S) in thiophosphate (P=S) analog II. The 2-5A compounds were synthesized, deprotected and purified as described herein utilizing CPG support with 3'-inverted abasic nucleotide. For chain extension 5'-O-(4,4'-dimethoxytrityl)-3'-O-(tert-butyldimethylsilyl)-N6-benzoyl-adenosine-2-cyanoethyl-N,N-diisopropylphosphoramidite (Chem. Genes Corp., Waltham, MA) was employed. Introduction of a 5'-terminal phosphate (analog I) or thiophosphate (analog II) group was performed with "Chemical Phosphorylation Reagent" (Glen Research, Sterling, VA). Structures of the final compounds were confirmed by MALDI-TOF analysis.

Figure 36 is a bar graph showing ribozyme activity and enhanced antiviral effect. (A) Interferon/ribozyme combination treatment. (B) 2-5A/ribozyme combination treatment. HeLa cells seeded in 96-well plates (10,000 cells per well) were pretreated as indicated for 4 hours. For pretreatment, SAC (RPI 17894), RZ (RPI 13919), and 2-5A analog I (RPI 21096) (200 nM) were complexed with lipid cytofectin. Cells were then infected with HCV-PV at a multiplicity of infection of 0.1. Virus inoculum was replaced after 30 minutes with media containing 5% serum and 100 nM RZ or SAC as indicated, complexed with cytofectin RPI.9778. After 20 hours, cells were lysed by 3 freeze/thaw cycles and virus was quantified by plaque assay. Plaque forming units (PFU)/ml are shown as the mean of triplicate samples + SEM. The absolute amount of viral yield in treated cells varied from day to day, presumably due to day to day variations in cell plating and transfection complexation. None, normal media; IFN, 10 U/ml consensus interferon; SAC, scrambled arm attenuated core control (RPI 17894); RZ, anti-HCV ribozyme (RPI 13919); 2-5A, (RPI 21096).

Figure 37 is a graph showing the inhibition of viral replication with anti-HCV ribozyme (RPI 13919) or 2-5A (RPI 21096) treatment. HeLa cells were treated as described

in **Figure 36** except that there was no pretreatment and 200 nM oligonucleotide was used for treatment. 2-5A P=S contains a 5'-terminal thiophosphate (RPI21095) (see **Figure 35**).

Figure 38 is a bar graph showing anti-HCV ribozyme in combination with 2-5A treatment. HeLa cells were treated as described in **Figure 37** except concentrations were co-varied as shown to maintain a constant 200 nM total oligonucleotide dose for transfection. Cells treated with 50 nM anti-HCV ribozyme (RPI 13919) (middle bars) were also treated with 150 nM SAC (RPI 17894) or 2-5A (RPI 21096); likewise, cells treated with 100 nM anti-HCV ribozyme (bars at right) were also treated with 100 nM SAC or 2-5A.

Mechanism of action of Nucleic Acid Molecules of the Invention

Decoy: Nucleic acid decoy molecules are mimetics of naturally occurring nucleic acid molecules or portions of naturally occurring nucleic acid molecules that can be used to modulate the function of a specific protein or a nucleic acid whose activity is dependant on interaction with the naturally occurring nucleic acid molecule. Decoys modulate the function of a target protein or nucleic acid by competing with authentic nucleic acid binding to the ligand of interest. Often, the nucleic acid decoy is a truncated version of a nucleic acid sequence that is recognized, for example by a particular protein, such as a transcription factor or polymerase. Decoys can be chemically modified to increase binding affinity to the target ligand as well as to increase the enzymatic and chemical stability of the decoy. In addition, bridging and non-bridging linkers can be introduced into the decoy sequence to provide additional binding affinity to the target ligand. Decoy molecules of the invention that bind to an HCV or HBV target, such as HBV reverse transcriptase or HBV reverse transcriptase primer, or an enhancer region of the HBV pregenomic RNA, for example the Enhancer I element, modulate the transcription of RNA to DNA and therefore modulate expression of the pregenomic RNA of the virus (see **Figures 13 and 14**).

Aptamer: Nucleic acid aptamers can be selected to specifically bind to a particular ligand of interest (see for example Gold *et al.*, US 5,567,588 and US 5,475,096, Gold *et al.*, 1995, *Annu. Rev. Biochem.*, 64, 763; Brody and Gold, 2000, *J. Biotechnol.*, 74, 5; Sun, 2000, *Curr. Opin. Mol. Ther.*, 2, 100; Kusser, 2000, *J. Biotechnol.*, 74, 27; Hermann and Patel, 2000, *Science*, 287, 820; and Jayasena, 1999, *Clinical Chemistry*, 45, 1628). For example, the use of in vitro selection can be applied to evolve nucleic acid aptamers with binding specificity for HBV RT and/or HBV RT primer. Nucleic acid aptamers can include chemical modifications and linkers as described herein. Aptamer molecules of the invention that bind to a reverse transcriptase or reverse transcriptase primer, such as HBV reverse transcriptase or HBV reverse transcriptase primer, modulate the transcription of RNA to DNA and therefore modulate expression of the pregenomic RNA of the virus.

Antisense: Antisense molecules can be modified or unmodified RNA, DNA, or mixed polymer oligonucleotides and primarily function by specifically binding to matching sequences resulting in modulation of peptide synthesis (Wu-Pong, Nov 1994, *BioPharm*, 20-33). The antisense oligonucleotide binds to target RNA by Watson Crick base-pairing and blocks gene expression by preventing ribosomal translation of the bound sequences either by steric blocking or by activating RNase H enzyme. Antisense molecules can also alter protein synthesis by interfering with RNA processing or transport from the nucleus into the cytoplasm (Mukhopadhyay & Roth, 1996, *Crit. Rev. in Oncogenesis* 7, 151-190).

In addition, binding of single stranded DNA to RNA may result in nuclease degradation of the heteroduplex (Wu-Pong, *supra*; Crooke, *supra*). To date, the only backbone modified DNA chemistry which will act as substrates for RNase H are phosphorothioates, phosphorodithioates, and borontrifluoridates. Recently, it has been reported that 2'-arabino and 2'-fluoro arabino- containing oligos can also activate RNase H activity.

A number of antisense molecules have been described that utilize novel configurations of chemically modified nucleotides, secondary structure, and/or RNase H substrate domains (Woolf *et al.*, International PCT Publication No. WO 98/13526; Thompson *et al.*, USSN 60/082,404 which was filed on April 20, 1998; Hartmann *et al.*, USSN 60/101,174 which was filed on September 21, 1998) all of these are incorporated by reference herein in their entirety.

Antisense DNA can be used to target RNA by means of DNA-RNA interactions, thereby activating RNase H, which digests the target RNA in the duplex. Antisense DNA can be chemically synthesized or can be expressed via the use of a single stranded DNA intracellular expression vector or the equivalent thereof.

Triplex Forming Oligonucleotides (TFO): Single stranded oligonucleotide can be designed to bind to genomic DNA in a sequence specific manner. TFOs can be comprised of pyrimidine-rich oligonucleotides which bind DNA helices through Hoogsteen Base-pairing (Wu-Pong, *supra*). In addition, TFOs can be chemically modified to increase binding affinity to target DNA sequences. The resulting triple helix composed of the DNA sense, DNA antisense, and TFO disrupts RNA synthesis by RNA polymerase. The TFO mechanism can result in gene expression or cell death since binding may be irreversible (Mukhopadhyay & Roth, *supra*)

2'-5' Oligoadenylates: The 2-5A system is an interferon-mediated mechanism for RNA degradation found in higher vertebrates (Mitra *et al.*, 1996, *Proc Nat Acad Sci USA* 93, 6780-6785). Two types of enzymes, 2-5A synthetase and RNase L, are required for RNA cleavage. The 2-5A synthetases require double stranded RNA to form 2'-5' oligoadenylates

(2-5A). 2-5A then acts as an allosteric effector for utilizing RNase L, which has the ability to cleave single stranded RNA. The ability to form 2-5A structures with double stranded RNA makes this system particularly useful for modulation of viral replication.

(2'-5') oligoadenylate structures can be covalently linked to antisense molecules to form chimeric oligonucleotides capable of RNA cleavage (Torrence, *supra*). These molecules putatively bind and activate a 2-5A-dependent RNase, the oligonucleotide/enzyme complex then binds to a target RNA molecule which can then be cleaved by the RNase enzyme. The covalent attachment of 2'-5' oligoadenylate structures is not limited to antisense applications, and can be further elaborated to include attachment to nucleic acid molecules of the instant invention.

RNA interference (RNAi): RNA interference refers to the process of sequence specific post transcriptional gene silencing in animals mediated by short interfering RNAs (siRNA) (Fire *et al.*, 1998, *Nature*, 391, 806). The corresponding process in plants is commonly referred to as post transcriptional gene silencing or RNA silencing and is also referred to as quelling in fungi. The process of post transcriptional gene silencing is thought to be an evolutionarily conserved cellular defense mechanism used to prevent the expression of foreign genes which is commonly shared by diverse flora and phyla (Fire *et al.*, 1999, *Trends Genet.*, 15, 358). Such protection from foreign gene expression may have evolved in response to the production of double stranded RNAs (dsRNA) derived from viral infection or the random integration of transposon elements into a host genome via a cellular response that specifically destroys homologous single stranded RNA or viral genomic RNA. The presence of dsRNA in cells triggers the RNAi response through a mechanism that has yet to be fully characterized. This mechanism appears to be different from the interferon response that results from dsRNA mediated activation of protein kinase PKR and 2',5'-oligoadenylate synthetase resulting in non-specific cleavage of mRNA by ribonuclease L.

The presence of long dsRNAs in cells stimulates the activity of a ribonuclease III enzyme referred to as dicer. Dicer is involved in the processing of the dsRNA into short pieces of dsRNA known as short interfering RNAs (siRNA) (Berstein *et al.*, 2001, *Nature*, 409, 363). Short interfering RNAs derived from dicer activity are typically about 21-23 nucleotides in length and comprise about 19 base pair duplexes. Dicer has also been implicated in the excision of 21 and 22 nucleotide small temporal RNAs (stRNA) from precursor RNA of conserved structure that are implicated in translational control (Hutvagner *et al.*, 2001, *Science*, 293, 834). The RNAi response also features an endonuclease complex containing a siRNA, commonly referred to as an RNA-induced silencing complex (RISC), which mediates cleavage of single stranded RNA having sequence homologous to the siRNA. Cleavage of the target RNA takes place in the middle of the region complementary to the guide sequence of the siRNA duplex (Elbashir *et al.*, 2001, *Genes Dev.*, 15, 188).

Short interfering RNA mediated RNAi has been studied in a variety of systems. Fire *et al.*, 1998, *Nature*, 391, 806, were the first to observe RNAi in *C. Elegans*. Wianny and Goetz, 1999, *Nature Cell Biol.*, 2, 70, describes RNAi mediated by dsRNA in mouse embryos. Hammond *et al.*, 2000, *Nature*, 404, 293, describe RNAi in *Drosophila* cells transfected with dsRNA. Elbashir *et al.*, 2001, *Nature*, 411, 494, describe RNAi induced by introduction of duplexes of synthetic 21-nucleotide RNAs in cultured mammalian cells including human embryonic kidney and HeLa cells. Recent work in *Drosophila* embryonic lysates has revealed certain requirements for siRNA length, structure, chemical composition, and sequence that are essential to mediate efficient RNAi activity. These studies have shown that 21 nucleotide siRNA duplexes are most active when containing two nucleotide 3'-overhangs. Furthermore, substitution of one or both siRNA strands with 2'-deoxy or 2'-O-methyl nucleotides abolishes RNAi activity, whereas substitution of 3'-terminal siRNA nucleotides with deoxy nucleotides was shown to be tolerated. Mismatch sequences in the center of the siRNA duplex were also shown to abolish RNAi activity. In addition, these studies also indicate that the position of the cleavage site in the target RNA is defined by the 5'-end of the siRNA guide sequence rather than the 3'-end (Elbashir *et al.*, 2001, *EMBO J.*, 20, 6877). Other studies have indicated that a 5'-phosphate on the target-complementary strand of a siRNA duplex is required for siRNA activity and that ATP is utilized to maintain the 5'-phosphate moiety on the siRNA (Nykanen *et al.*, 2001, *Cell*, 107, 309), however siRNA molecules lacking a 5'-phosphate are active when introduced exogenously, suggesting that 5'-phosphorylation of siRNA constructs may occur *in vivo*.

Enzymatic Nucleic Acid: Several varieties of naturally occurring enzymatic RNAs are presently known (Doherty and Doudna, 2001, *Annu. Rev. Biophys. Biomol. Struct.*, 30, 457-475; Symons, 1994, *Curr. Opin. Struct. Biol.*, 4, 322-30). In addition, several *in vitro* selection (evolution) strategies (Orgel, 1979, *Proc. R. Soc. London*, B 205, 435) have been used to evolve new nucleic acid catalysts capable of catalyzing cleavage and ligation of phosphodiester linkages (Joyce, 1989, *Gene*, 82, 83-87; Beaudry *et al.*, 1992, *Science* 257, 635-641; Joyce, 1992, *Scientific American* 267, 90-97; Breaker *et al.*, 1994, *TIBTECH* 12, 268; Bartel *et al.*, 1993, *Science* 261:1411-1418; Szostak, 1993, *TIBS* 17, 89-93; Kumar *et al.*, 1995, *FASEB J.*, 9, 1183; Breaker, 1996, *Curr. Op. Biotech.*, 7, 442; Santoro *et al.*, 1997, *Proc. Natl. Acad. Sci.*, 94, 4262; Tang *et al.*, 1997, *RNA* 3, 914; Nakamaye & Eckstein, 1994, *supra*; Long & Uhlenbeck, 1994, *supra*; Ishizaka *et al.*, 1995, *supra*; Vaish *et al.*, 1997, *Biochemistry* 36, 6495). Each can catalyze a series of reactions including the hydrolysis of phosphodiester bonds in *trans* (and thus can cleave other RNA molecules) under physiological conditions.

Nucleic acid molecules of this invention can block HBV or HCV protein expression and can be used to treat disease or diagnose disease associated with the levels of HBV or HCV.

The enzymatic nature of an enzymatic nucleic acid has significant advantages, such as the concentration of nucleic acid necessary to affect a therapeutic treatment is low. This advantage reflects the ability of the enzymatic nucleic acid molecule to act enzymatically. Thus, a single enzymatic nucleic acid molecule is able to cleave many molecules of target RNA. In addition, the enzymatic nucleic acid molecule is a highly specific modulator, with the specificity of modulation depending not only on the base-pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can be chosen to completely eliminate catalytic activity of an enzymatic nucleic acid molecule.

Nucleic acid molecules having an endonuclease enzymatic activity are able to repeatedly cleave other separate RNA molecules in a nucleotide base sequence-specific manner. With proper design and construction, such enzymatic nucleic acid molecules can be targeted to any RNA transcript, and efficient cleavage achieved *in vitro* (Zaug *et al.*, 324, *Nature* 429 1986; Uhlenbeck, 1987 *Nature* 328, 596; Kim *et al.*, 84 *Proc. Natl. Acad. Sci. USA* 8788, 1987; Dreyfus, 1988, *Einstein Quart. J. Bio. Med.*, 6, 92; Haseloff and Gerlach, 334 *Nature* 585, 1988; Cech, 260 *JAMA* 3030, 1988; and Jefferies *et al.*, 17 *Nucleic Acids Research* 1371, 1989; Chartrand *et al.*, 1995, *Nucleic Acids Research* 23, 4092; Santoro *et al.*, 1997, *PNAS* 94, 4262).

Because of their sequence specificity, *trans*-cleaving enzymatic nucleic acid molecules show promise as therapeutic agents for human disease (Usman & McSwiggen, 1995 *Ann. Rep. Med. Chem.* 30, 285-294; Christoffersen and Marr, 1995 *J. Med. Chem.* 38, 2023-2037). Enzymatic nucleic acid molecule can be designed to cleave specific RNA targets within the background of cellular RNA. Such a cleavage event renders the RNA non-functional and abrogates protein expression from that RNA. In this manner, synthesis of a protein associated with a disease state can be selectively modulated (Warashina *et al.*, 1999, *Chemistry and Biology*, 6, 237-250).

The present invention also features nucleic acid sensor molecules or allozymes having sensor domains comprising nucleic acid decoys and/or aptamers of the invention. Interaction of the nucleic acid sensor molecule's sensor domain with a molecular target, such as HCV or HBV target, e.g., HBV RT and/or HBV RT primer, can activate or inactivate the enzymatic nucleic acid domain of the nucleic acid sensor molecule, such that the activity of the nucleic acid sensor molecule is modulated in the presence of the target-signaling molecule. The nucleic acid sensor molecule can be designed to be active in the presence of the target

molecule or alternately, can be designed to be inactive in the presence of the molecular target. For example, a nucleic acid sensor molecule is designed with a sensor domain having the sequence (UUCA)_n, where n is an integer from 1-10. In a non-limiting example, interaction of the HBV RT primer with the sensor domain of the nucleic acid sensor molecule can activate the enzymatic nucleic acid domain of the nucleic acid sensor molecule such that the sensor molecule catalyzes a reaction, for example cleavage of HBV RNA. In this example, the nucleic acid sensor molecule is activated in the presence of HBV RT or HBV RT primer, and can be used as a therapeutic to treat HBV infection. Alternately, the reaction can comprise cleavage or ligation of a labeled nucleic acid reporter molecule, providing a useful diagnostic reagent to detect the presence of HBV in a system.

HCV Target sites

Targets for useful nucleic acid molecules and nuclease activating compounds or chimeras can be determined as disclosed in Draper *et al.*, WO 93/23569; Sullivan *et al.*, WO 93/23057; Thompson *et al.*, WO 94/02595; Draper *et al.*, WO 95/04818; McSwiggen *et al.*, US Patent No. 5,525,468. Rather than repeat the guidance provided in those documents here, below are provided specific examples of such methods, not limiting to those in the art. Nucleic acid molecules and nuclease activating compounds or chimeras to such targets are designed as described in those applications and synthesized to be tested *in vitro* and *in vivo*, as also described. Such nucleic acid molecules and nuclease activating compounds or chimeras can also be optimized and delivered as described therein.

The sequence of HCV RNAs were screened for optimal enzymatic nucleic acid molecule target sites using a computer folding algorithm. Enzymatic nucleic acid cleavage sites were identified. These sites are shown in **Tables XVIII, XIX, XX and XXIII** (All sequences are 5' to 3' in the tables). The nucleotide base position is noted in the tables as that site to be cleaved by the designated type of enzymatic nucleic acid molecule. The nucleotide base position is noted in the tables as that site to be cleaved by the designated type of enzymatic nucleic acid molecule.

Because HCV RNAs are highly homologous in certain regions, some enzymatic nucleic acid molecule target sites are also homologous. In this case, a single enzymatic nucleic acid molecule will target different classes of HCV RNA. The advantage of one enzymatic nucleic acid molecule that targets several classes of HCV RNA is clear, especially in cases where one or more of these RNAs can contribute to the disease state.

Enzymatic nucleic acid molecules were designed that could bind and were individually analyzed by computer folding (Jaeger *et al.*, 1989 *Proc. Natl. Acad. Sci. USA*, 86, 7706) to assess whether the enzymatic nucleic acid molecule sequences fold into the appropriate

secondary structure. Those enzymatic nucleic acid molecules with unfavorable intramolecular interactions between the binding arms and the catalytic core are eliminated from consideration. Varying binding arm lengths can be chosen to optimize activity. Generally, at least 5 bases on each arm are able to bind to, or otherwise interact with, the target RNA. Enzymatic nucleic acid molecules were designed to anneal to various sites in the mRNA message. The binding arms are complementary to the target site sequences described above.

HBV Target sites

Targets for useful ribozymes and antisense nucleic acids targeting HBV can be determined as disclosed in Draper *et al.*, WO 93/23569; Sullivan *et al.*, WO 93/23057; Thompson *et al.*, WO 94/02595; Draper *et al.*, WO 95/04818; McSwiggen *et al.*, US Patent No. 5,525,468. Other examples include the following PCT applications, which concern inactivation of expression of disease-related genes: WO 95/23225, WO 95/13380, WO 94/02595. Rather than repeat the guidance provided in those documents here, below are provided specific examples of such methods, not limiting to those in the art. Ribozymes and antisense to such targets are designed as described in those applications and synthesized to be tested *in vitro* and *in vivo*, as also described. The sequence of human HBV RNAs (for example, accession AF100308.1; HBV strain 2-18; additionally, other HBV strains can be screened by one skilled in the art, see **Table III** for other possible strains) were screened for optimal enzymatic nucleic acid and antisense target sites using a computer-folding algorithm. Antisense, hammerhead, DNAzyme, NCH (Inozyme), amberzyme, zinzyme or G-Cleaver ribozyme binding/cleavage sites were identified. These sites are shown in **Tables V to XI** (all sequences are 5' to 3' in the tables; X can be any base-paired sequence, the actual sequence is not relevant here). The nucleotide base position is noted in the Tables as that site to be cleaved by the designated type of enzymatic nucleic acid molecule. **Table IV** shows substrate positions selected from Renbo *et al.*, 1987, *Sci. Sin.*, 30, 507, used in Draper, USSN (07/882,712), filed May 14, 1992, entitled "METHOD AND REAGENT FOR INHIBITING HEPATITIS B VIRUS REPLICATION" and Draper *et al.*, International PCT publication No. WO 93/23569, filed April 29, 1993, entitled "METHOD AND REAGENT FOR INHIBITING VIRAL REPLICATION". While human sequences can be screened and enzymatic nucleic acid molecule and/or antisense thereafter designed, as discussed in Stinchcomb *et al.*, WO 95/23225, mouse targeted ribozymes can be useful to test efficacy of action of the enzymatic nucleic acid molecule and/or antisense prior to testing in humans.

Antisense, hammerhead, DNAzyme, NCH (Inozyme), amberzyme, zinzyme or G-Cleaver ribozyme binding/cleavage sites were identified, as discussed above. The nucleic acid molecules were individually analyzed by computer folding (Jaeger *et al.*, 1989 *Proc.*

Natl. Acad. Sci. USA, 86, 7706) to assess whether the sequences fold into the appropriate secondary structure. Those nucleic acid molecules with unfavorable intramolecular interactions such as between the binding arms and the catalytic core were eliminated from consideration. Varying binding arm lengths can be chosen to optimize activity.

5 Antisense, hammerhead, DNAzyme, NCH, amberzyme, zinzyme or G-Cleaver ribozyme binding/cleavage sites were identified and were designed to anneal to various sites in the RNA target. The binding arms are complementary to the target site sequences described above. The nucleic acid molecules were chemically synthesized. The method of synthesis used follows the procedure for normal DNA/RNA synthesis as described below and
10 in Usman *et al.*, 1987 *J. Am. Chem. Soc.*, 109, 7845; Scaringe *et al.*, 1990 *Nucleic Acids Res.*, 18, 5433; Wincott *et al.*, 1995 *Nucleic Acids Res.* 23, 2677-2684; and Caruthers *et al.*, 1992, *Methods in Enzymology* 211,3-19.

Synthesis of Nucleic acid Molecules

15 Synthesis of nucleic acids greater than 100 nucleotides in length is difficult using automated methods, and the therapeutic cost of such molecules is prohibitive. In this invention, small nucleic acid motifs ("small" refers to nucleic acid motifs no more than 100 nucleotides in length, preferably no more than 80 nucleotides in length, and most preferably no more than 50 nucleotides in length; *e.g.*, decoy nucleic acid molecules, aptamer nucleic acid molecules antisense nucleic acid molecules, enzymatic nucleic acid molecules) are
20 preferably used for exogenous delivery. The simple structure of these molecules increases the ability of the nucleic acid to invade targeted regions of protein and/or RNA structure. Exemplary molecules of the instant invention are chemically synthesized, and others can similarly be synthesized.

Oligonucleotides (*e.g.*, DNA oligonucleotides) are synthesized using protocols known
25 in the art, for example as described in Caruthers *et al.*, 1992, *Methods in Enzymology* 211, 3-19, Thompson *et al.*, International PCT Publication No. WO 99/54459, Wincott *et al.*, 1995, *Nucleic Acids Res.* 23, 2677-2684, Wincott *et al.*, 1997, *Methods Mol. Bio.*, 74, 59, Brennan *et al.*, 1998, *Biotechnol Bioeng.*, 61, 33-45, and Brennan, US patent No. 6,001,311. The synthesis of oligonucleotides makes use of common nucleic acid protecting and coupling
30 groups, such as dimethoxytrityl at the 5'-end, and phosphoramidites at the 3'-end. In a non-limiting example, small scale syntheses are conducted on a 394 Applied Biosystems, Inc. synthesizer using a 0.2 μ mol scale protocol with a 2.5 min coupling step for 2'-O-methylated nucleotides and a 45 sec coupling step for 2'-deoxy nucleotides. **Table II** outlines the amounts and the contact times of the reagents used in the synthesis cycle. Alternatively,
35 syntheses at the 0.2 μ mol scale can be performed on a 96-well plate synthesizer, such as the instrument produced by Protogene (Palo Alto, CA) with minimal modification to the cycle.

A 33-fold excess (60 μ L of 0.11 M = 6.6 μ mol) of 2'-O-methyl phosphoramidite and a 105-fold excess of S-ethyl tetrazole (60 μ L of 0.25 M = 15 μ mol) can be used in each coupling cycle of 2'-O-methyl residues relative to polymer-bound 5'-hydroxyl. A 22-fold excess (40 μ L of 0.11 M = 4.4 μ mol) of deoxy phosphoramidite and a 70-fold excess of S-ethyl tetrazole (40 μ L of 0.25 M = 10 μ mol) can be used in each coupling cycle of deoxy residues relative to polymer-bound 5'-hydroxyl. Average coupling yields on the 394 Applied Biosystems, Inc. synthesizer, determined by colorimetric quantitation of the trityl fractions, are typically 97.5-99%. Other oligonucleotide synthesis reagents for the 394 Applied Biosystems, Inc. synthesizer include the following: detritylation solution is 3% TCA in methylene chloride (ABI); capping is performed with 16% *N*-methyl imidazole in THF (ABI) and 10% acetic anhydride/10% 2,6-lutidine in THF (ABI); and oxidation solution is 16.9 mM I₂, 49 mM pyridine, 9% water in THF (PERSEPTIVE™). Burdick & Jackson Synthesis Grade acetonitrile is used directly from the reagent bottle. S-Ethyltetrazole solution (0.25 M in acetonitrile) is made up from the solid obtained from American International Chemical, Inc. Alternately, for the introduction of phosphorothioate linkages, Beaucage reagent (3H-1,2-Benzodithiol-3-one 1,1-dioxide, 0.05 M in acetonitrile) is used.

Deprotection of the DNA-based oligonucleotides is performed as follows: the polymer-bound trityl-on oligoribonucleotide is transferred to a 4 mL glass screw top vial and suspended in a solution of 40% aq. methylamine (1 mL) at 65 °C for 10 min. After cooling to -20 °C, the supernatant is removed from the polymer support. The support is washed three times with 1.0 mL of EtOH:MeCN:H₂O/3:1:1, vortexed and the supernatant is then added to the first supernatant. The combined supernatants, containing the oligoribonucleotide, are dried to a white powder.

The method of synthesis used for normal RNA including certain decoy nucleic acid molecules and enzymatic nucleic acid molecules follows the procedure as described in Usman *et al.*, 1987, *J. Am. Chem. Soc.*, 109, 7845; Scaringe *et al.*, 1990, *Nucleic Acids Res.*, 18, 5433; and Wincott *et al.*, 1995, *Nucleic Acids Res.* 23, 2677-2684 Wincott *et al.*, 1997, *Methods Mol. Bio.*, 74, 59, and makes use of common nucleic acid protecting and coupling groups, such as dimethoxytrityl at the 5'-end, and phosphoramidites at the 3'-end. In a non-limiting example, small scale syntheses are conducted on a 394 Applied Biosystems, Inc. synthesizer using a 0.2 μ mol scale protocol with a 7.5 min coupling step for alkylsilyl protected nucleotides and a 2.5 min coupling step for 2'-O-methylated nucleotides. **Table II** outlines the amounts and the contact times of the reagents used in the synthesis cycle. Alternatively, syntheses at the 0.2 μ mol scale can be done on a 96-well plate synthesizer, such as the instrument produced by Protogene (Palo Alto, CA) with minimal modification to the cycle. A 33-fold excess (60 μ L of 0.11 M = 6.6 μ mol) of 2'-O-methyl phosphoramidite and a 75-fold excess of S-ethyl tetrazole (60 μ L of 0.25 M = 15 μ mol) can be used in each

coupling cycle of 2'-O-methyl residues relative to polymer-bound 5'-hydroxyl. A 66-fold excess (120 μ L of 0.11 M = 13.2 μ mol) of alkylsilyl (ribo) protected phosphoramidite and a 150-fold excess of S-ethyl tetrazole (120 μ L of 0.25 M = 30 μ mol) can be used in each coupling cycle of ribo residues relative to polymer-bound 5'-hydroxyl. Average coupling yields on the 394 Applied Biosystems, Inc. synthesizer, determined by colorimetric quantitation of the trityl fractions, are typically 97.5-99%. Other oligonucleotide synthesis reagents for the 394 Applied Biosystems, Inc. synthesizer include the following: detritylation solution is 3% TCA in methylene chloride (ABI); capping is performed with 16% *N*-methyl imidazole in THF (ABI) and 10% acetic anhydride/10% 2,6-lutidine in THF (ABI); oxidation solution is 16.9 mM I₂, 49 mM pyridine, 9% water in THF (PERSEPTIVE™). Burdick & Jackson Synthesis Grade acetonitrile is used directly from the reagent bottle. S-Ethyltetrazole solution (0.25 M in acetonitrile) is made up from the solid obtained from American International Chemical, Inc. Alternately, for the introduction of phosphorothioate linkages, Beaucage reagent (3H-1,2-Benzodithiol-3-one 1,1-dioxide 0.05 M in acetonitrile) is used.

Deprotection of the RNA is performed using either a two-pot or one-pot protocol. For the two-pot protocol, the polymer-bound trityl-on oligoribonucleotide is transferred to a 4 mL glass screw top vial and suspended in a solution of 40% aq. methylamine (1 mL) at 65 °C for 10 min. After cooling to -20 °C, the supernatant is removed from the polymer support. The support is washed three times with 1.0 mL of EtOH:MeCN:H₂O/3:1:1, vortexed and the supernatant is then added to the first supernatant. The combined supernatants, containing the oligoribonucleotide, are dried to a white powder. The base deprotected oligoribonucleotide is resuspended in anhydrous TEA/HF/NMP solution (300 μ L of a solution of 1.5 mL *N*-methylpyrrolidinone, 750 μ L TEA and 1 mL TEA•3HF to provide a 1.4 M HF concentration) and heated to 65 °C. After 1.5 h, the oligomer is quenched with 1.5 M NH₄HCO₃.

Alternatively, for the one-pot protocol, the polymer-bound trityl-on oligoribonucleotide is transferred to a 4 mL glass screw top vial and suspended in a solution of 33% ethanolic methylamine/DMSO: 1/1 (0.8 mL) at 65 °C for 15 min. The vial is brought to r.t. TEA•3HF (0.1 mL) is added and the vial is heated at 65 °C for 15 min. The sample is cooled at -20 °C and then quenched with 1.5 M NH₄HCO₃.

For purification of the trityl-on oligomers, the quenched NH₄HCO₃ solution is loaded onto a C-18 containing cartridge that had been prewashed with acetonitrile followed by 50 mM TEAA. After washing the loaded cartridge with water, the RNA is detritylated with 0.5% TFA for 13 min. The cartridge is then washed again with water, salt exchanged with 1 M NaCl and washed with water again. The oligonucleotide is then eluted with 30% acetonitrile.

Inactive hammerhead ribozymes or binding attenuated control (BAC) oligonucleotides are synthesized by substituting a U for G₅ and a U for A₁₄ (numbering from Hertel, K. J., *et al.*, 1992, *Nucleic Acids Res.*, 20, 3252). Similarly, one or more nucleotide substitutions can be introduced in other nucleic acid decoy molecules to inactivate the molecule and such molecules can serve as a negative control.

The average stepwise coupling yields are typically >98% (Wincott *et al.*, 1995 *Nucleic Acids Res.* 23, 2677-2684). Those of ordinary skill in the art will recognize that the scale of synthesis can be adapted to be larger or smaller than the example described above including but not limited to 96-well format, all that is important is the ratio of chemicals used in the reaction.

Alternatively, the nucleic acid molecules of the present invention can be synthesized separately and joined together post-synthetically, for example, by ligation (Moore *et al.*, 1992, *Science* 256, 9923; Draper *et al.*, International PCT publication No. WO 93/23569; Shabarova *et al.*, 1991, *Nucleic Acids Research* 19, 4247; Bellon *et al.*, 1997, *Nucleosides & Nucleotides*, 16, 951; Bellon *et al.*, 1997, *Bioconjugate Chem.* 8, 204).

The nucleic acid molecules of the present invention can be modified extensively to enhance stability by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-fluoro, 2'-O-methyl, 2'-H (for a review see Usman and Cedergren, 1992, *TIBS* 17, 34; Usman *et al.*, 1994, *Nucleic Acids Symp. Ser.* 31, 163). Ribozymes can be purified by gel electrophoresis using general methods or can be purified by high pressure liquid chromatography (HPLC; see Wincott *et al.*, *supra*, the totality of which is hereby incorporated herein by reference) and re-suspended in water.

The sequences of the nucleic acid molecules that are chemically synthesized, useful in this study, are shown in **Tables XI, XV, XX, XXI, XXII and XXIII**. The nucleic acid sequences listed in **Tables IV-XI, XIV-XV and XVIII-XXIII** can be formed of ribonucleotides or other nucleotides or non-nucleotides. Such nucleic acid sequences are equivalent to the sequences described specifically in the Tables.

Optimizing Activity of the nucleic acid molecule of the invention

Chemically synthesizing nucleic acid molecules with modifications (base, sugar and/or phosphate) can prevent their degradation by serum ribonucleases, which can increase their potency (see *e.g.*, Eckstein *et al.*, International Publication No. WO 92/07065; Perrault *et al.*, 1990 *Nature* 344, 565; Pieken *et al.*, 1991, *Science* 253, 314; Usman and Cedergren, 1992, *Trends in Biochem. Sci.* 17, 334; Usman *et al.*, International Publication No. WO 93/15187; and Rossi *et al.*, International Publication No. WO 91/03162; Sproat, US Patent No.

5,334,711; Gold *et al.*, US 6,300,074; and Burgin *et al.*, *supra*; all of which are incorporated by reference herein). All of the above references describe various chemical modifications that can be made to the base, phosphate and/or sugar moieties of the nucleic acid molecules described herein. Modifications that enhance their efficacy in cells, and removal of bases from nucleic acid molecules to shorten oligonucleotide synthesis times and reduce chemical requirements are desired.

There are several examples in the art describing sugar, base and phosphate modifications that can be introduced into nucleic acid molecules with significant enhancement in their nuclease stability and efficacy. For example, oligonucleotides are modified to enhance stability and/or enhance biological activity by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-fluoro, 2'-O-methyl, 2'-H, nucleotide base modifications (for a review see Usman and Cedergren, 1992, *TIBS*, 17, 34; Usman *et al.*, 1994, *Nucleic Acids Symp. Ser.* 31, 163; Burgin *et al.*, 1996, *Biochemistry*, 35, 14090). Sugar modification of nucleic acid molecules have been extensively described in the art (see Eckstein *et al.*, *International Publication* PCT No. WO 92/07065; Perrault *et al.* *Nature*, 1990, 344, 565-568; Pieken *et al.* *Science*, 1991, 253, 314-317; Usman and Cedergren, *Trends in Biochem. Sci.*, 1992, 17, 334-339; Usman *et al.* *International Publication* PCT No. WO 93/15187; Sproat, *US Patent* No. 5,334,711 and Beigelman *et al.*, 1995, *J. Biol. Chem.*, 270, 25702; Beigelman *et al.*, *International PCT publication* No. WO 97/26270; Beigelman *et al.*, *US Patent* No. 5,716,824; Usman *et al.*, *US patent* No. 5,627,053; Woolf *et al.*, *International PCT Publication* No. WO 98/13526; Thompson *et al.*, *USSN* 60/082,404 which was filed on April 20, 1998; Karpeisky *et al.*, 1998, *Tetrahedron Lett.*, 39, 1131; Earnshaw and Gait, 1998, *Biopolymers (Nucleic Acid Sciences)*, 48, 39-55; Verma and Eckstein, 1998, *Annu. Rev. Biochem.*, 67, 99-134; and Burlina *et al.*, 1997, *Bioorg. Med. Chem.*, 5, 1999-2010; all of the references are hereby incorporated in their totality by reference herein). Such publications describe general methods and strategies to determine the location of incorporation of sugar, base and/or phosphate modifications and the like into ribozymes without modulating catalysis, and are incorporated by reference herein. In view of such teachings, similar modifications can be used as described herein to modify the nucleic acid molecules of the instant invention.

While chemical modification of oligonucleotide internucleotide linkages with phosphorothioate, phosphorothioate, and/or 5'-methylphosphonate linkages improves stability, excessive modifications can cause some toxicity. Therefore, when designing nucleic acid molecules, the amount of these internucleotide linkages should be minimized. The reduction in the concentration of these linkages should lower toxicity, resulting in increased efficacy and higher specificity of these molecules.

Nucleic acid molecules having chemical modifications that maintain or enhance activity are provided. Such a nucleic acid is also generally more resistant to nucleases than an unmodified nucleic acid. Accordingly, the *in vitro* and/or *in vivo* activity should not be significantly lowered. In cases in which modulation is the goal, therapeutic nucleic acid molecules delivered exogenously should optimally be stable within cells until translation of the target RNA has been modulated long enough to reduce the levels of the undesirable protein. This period of time varies between hours to days depending upon the disease state. Improvements in the chemical synthesis of RNA and DNA (Wincott *et al.*, 1995 *Nucleic Acids Res.* 23, 2677; Caruthers *et al.*, 1992, *Methods in Enzymology* 211,3-19 (incorporated by reference herein)) have expanded the ability to modify nucleic acid molecules by introducing nucleotide modifications to enhance their nuclease stability, as described above.

In one embodiment, nucleic acid molecules of the invention include one or more G-clamp nucleotides. A G-clamp nucleotide is a modified cytosine analog wherein the modifications confer the ability to hydrogen bond both Watson-Crick and Hoogsteen faces of a complementary guanine within a duplex, see for example Lin and Matteucci, 1998, *J. Am. Chem. Soc.*, 120, 8531-8532. A single G-clamp analog substitution within an oligonucleotide can result in substantially enhanced helical thermal stability and mismatch discrimination when hybridized to complementary oligonucleotides. The inclusion of such nucleotides in nucleic acid molecules of the invention results in both enhanced affinity and specificity to nucleic acid targets. In another embodiment, nucleic acid molecules of the invention include one or more LNA "locked nucleic acid" nucleotides such as a 2', 4'-C methylene bicyclo nucleotide (see for example Wengel *et al.*, International PCT Publication No. WO 00/66604 and WO 99/14226).

In another embodiment, the invention features conjugates and/or complexes of nucleic acid molecules targeting HBV or HCV. Such conjugates and/or complexes can be used to facilitate delivery of molecules into a biological system, such as a cell. The conjugates and complexes provided by the instant invention can impart therapeutic activity by transferring therapeutic compounds across cellular membranes, altering the pharmacokinetics, and/or modulating the localization of nucleic acid molecules of the invention. The present invention encompasses the design and synthesis of novel conjugates and complexes for the delivery of molecules, including, but not limited to, small molecules, lipids, phospholipids, nucleosides, nucleotides, nucleic acids, antibodies, toxins, negatively charged polymers and other polymers, for example proteins, peptides, hormones, carbohydrates, polyethylene glycols, or polyamines, across cellular membranes. In general, the transporters described are designed to be used either individually or as part of a multi-component system, with or without degradable linkers. These compounds are expected to improve delivery and/or localization of nucleic acid molecules of the invention into a number of cell types originating from different

tissues, in the presence or absence of serum (see Sullenger and Cech, US 5,854,038). Conjugates of the molecules described herein can be attached to biologically active molecules via linkers that are biodegradable, such as biodegradable nucleic acid linker molecules.

5 The term “biodegradable nucleic acid linker molecule” as used herein, refers to a nucleic acid molecule that is designed as a biodegradable linker to connect one molecule to another molecule, for example, a biologically active molecule. The stability of the biodegradable nucleic acid linker molecule can be modulated by using various combinations of ribonucleotides, deoxyribonucleotides, and chemically modified nucleotides, for example, 2’-O-methyl, 2’-fluoro, 2’-amino, 2’-O-amino, 2’-C-allyl, 2’-O-allyl, and other 2’-modified
10 or base modified nucleotides. The biodegradable nucleic acid linker molecule can be a dimer, trimer, tetramer or longer nucleic acid molecule, for example, an oligonucleotide of about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides in length, or can comprise a single nucleotide with a phosphorus-based linkage, for example, a phosphoramidate or phosphodiester linkage. The biodegradable nucleic acid linker molecule
15 can also comprise nucleic acid backbone, nucleic acid sugar, or nucleic acid base modifications.

The term “biodegradable” as used herein, refers to degradation in a biological system, for example enzymatic degradation or chemical degradation.

20 The term “biologically active molecule” as used herein, refers to compounds or molecules that are capable of eliciting or modifying a biological response in a system. Non-limiting examples of biologically active molecules contemplated by the instant invention include therapeutically active molecules such as antibodies, hormones, antivirals, peptides, proteins, chemotherapeutics, small molecules, vitamins, co-factors, nucleosides, nucleotides, oligonucleotides, enzymatic nucleic acids, antisense nucleic acids, triplex forming
25 oligonucleotides, 2,5-A chimeras, siRNA, dsRNA, allozymes, aptamers, decoys and analogs thereof. Biologically active molecules of the invention also include molecules capable of modulating the pharmacokinetics and/or pharmacodynamics of other biologically active molecules, for example, lipids and polymers such as polyamines, polyamides, polyethylene glycol and other polyethers.

30 The term “phospholipid” as used herein, refers to a hydrophobic molecule comprising at least one phosphorus group. For example, a phospholipid can comprise a phosphorus-containing group and saturated or unsaturated alkyl group, optionally substituted with OH, COOH, oxo, amine, or substituted or unsubstituted aryl groups.

35 Therapeutic nucleic acid molecules (e.g., decoy nucleic acid molecules) delivered exogenously optimally are stable within cells until reverse transcription of the pregenomic

RNA has been modulated long enough to reduce the levels of HBV or HCV DNA. The nucleic acid molecules are resistant to nucleases in order to function as effective intracellular therapeutic agents. Improvements in the chemical synthesis of nucleic acid molecules described in the instant invention and in the art have expanded the ability to modify nucleic acid molecules by introducing nucleotide modifications to enhance their nuclease stability as described above.

In yet another embodiment, nucleic acid molecules having chemical modifications that maintain or enhance enzymatic activity are provided. Such nucleic acids are also generally more resistant to nucleases than unmodified nucleic acids. Thus, *in vitro* and/or *in vivo* the activity should not be significantly lowered. As exemplified herein, such nucleic acid molecules are useful *in vitro* and/or *in vivo* even if activity over all is reduced 10 fold (Burgin *et al.*, 1996, *Biochemistry*, 35, 14090).

Use of the nucleic acid-based molecules of the invention will lead to better treatment of the disease progression by affording the possibility of combination therapies (*e.g.*, multiple antisense, nucleic acid decoy, or nucleic acid aptamer molecules targeted to different genes; nucleic acid molecules coupled with known small molecule modulators or; or intermittent treatment with combinations of molecules (including different motifs) and/or other chemical or biological molecules). The treatment of patients with nucleic acid molecules may also include combinations of different types of nucleic acid molecules.

In another aspect the nucleic acid molecules comprise a 5' and/or a 3'- cap structure.

By "cap structure" is meant chemical modifications, which have been incorporated at either terminus of the oligonucleotide (see, for example, Wincott *et al.*, WO 97/26270, incorporated by reference herein). These terminal modifications protect the nucleic acid molecule from exonuclease degradation, and may help in delivery and/or localization within a cell. The cap may be present at the 5'-terminus (5'-cap) or at the 3'-terminal (3'-cap) or may be present on both termini. In non-limiting examples: the 5'-cap is selected from the group comprising inverted abasic residue (moiety); 4',5'-methylene nucleotide; 1-(beta-D-erythrofuransyl) nucleotide, 4'-thio nucleotide; carbocyclic nucleotide; 1,5-anhydrohexitol nucleotide; L-nucleotides; alpha-nucleotides; modified base nucleotide; phosphorodithioate linkage; *threo*-pentofuransyl nucleotide; acyclic 3',4'-seco nucleotide; acyclic 3,4-dihydroxybutyl nucleotide; acyclic 3,5-dihydroxypentyl nucleotide, 3'-3'-inverted nucleotide moiety; 3'-3'-inverted abasic moiety; 3'-2'-inverted nucleotide moiety; 3'-2'-inverted abasic moiety; 1,4-butanediol phosphate; 3'-phosphoramidate; hexylphosphate; aminohexyl phosphate; 3'-phosphate; 3'-phosphorothioate; phosphorodithioate; or bridging or non-bridging methylphosphonate moiety (for more details, see Wincott *et al.*, International PCT publication No. WO 97/26270, incorporated by reference herein).

In yet another preferred embodiment, the 3'-cap is selected from a group comprising, 4',5'-methylene nucleotide; 1-(beta-D-erythrofuransyl) nucleotide; 4'-thio nucleotide, carbocyclic nucleotide; 5'-amino-alkyl phosphate; 1,3-diamino-2-propyl phosphate; 3-aminopropyl phosphate; 6-aminohexyl phosphate; 1,2-aminododecyl phosphate; 5 hydroxypropyl phosphate; 1,5-anhydrohexitol nucleotide; L-nucleotide; alpha-nucleotide; modified base nucleotide; phosphorodithioate; *threo*-pentofuransyl nucleotide; acyclic 3',4'-seco nucleotide; 3,4-dihydroxybutyl nucleotide; 3,5-dihydroxypentyl nucleotide, 5'-5'-inverted nucleotide moiety; 5'-5'-inverted abasic moiety; 5'-phosphoramidate; 5'-phosphorothioate; 1,4-butanediol phosphate; 5'-amino; bridging and/or non-bridging 5'-phosphoramidate, phosphorothioate and/or phosphorodithioate, bridging or non bridging methylphosphonate and 5'-mercapto moieties (for more details see Beaucage and Iyer, 1993, *Tetrahedron* 49, 1925; incorporated by reference herein).

By the term "non-nucleotide" is meant any group or compound which can be incorporated into a nucleic acid chain in the place of one or more nucleotide units, including either sugar and/or phosphate substitutions, and allows the remaining bases to exhibit their enzymatic activity. The group or compound is abasic in that it does not contain a commonly recognized nucleotide base, such as adenosine, guanine, cytosine, uracil or thymine.

The term "alkyl" as used herein refers to a saturated aliphatic hydrocarbon, including straight-chain, branched-chain "isoalkyl", and cyclic alkyl groups. The term "alkyl" also comprises alkoxy, alkyl-thio, alkyl-thio-alkyl, alkoxyalkyl, alkylamino, alkenyl, alkynyl, alkoxy, cycloalkenyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, C1-C6 hydrocarbyl, aryl or substituted aryl groups. Preferably, the alkyl group has 1 to 12 carbons. More preferably it is a lower alkyl of from about 1 to 7 carbons, more preferably about 1 to 4 carbons. The alkyl group can be substituted or unsubstituted. When substituted the substituted group(s) preferably comprise hydroxy, oxy, thio, amino, nitro, cyano, alkoxy, alkyl-thio, alkyl-thio-alkyl, alkoxyalkyl, alkylamino, silyl, alkenyl, alkynyl, alkoxy, cycloalkenyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, C1-C6 hydrocarbyl, aryl or substituted aryl groups. The term "alkyl" also includes alkenyl groups containing at least one carbon-carbon double bond, including straight-chain, branched-chain, and cyclic groups. Preferably, the alkenyl group has about 2 to 12 carbons. More preferably it is a lower alkenyl of from about 2 to 7 carbons, more preferably about 2 to 4 carbons. The alkenyl group can be substituted or unsubstituted. When substituted the substituted group(s) preferably comprise hydroxy, oxy, thio, amino, nitro, cyano, alkoxy, alkyl-thio, alkyl-thio-alkyl, alkoxyalkyl, alkylamino, silyl, alkenyl, alkynyl, alkoxy, cycloalkenyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, C1-C6 hydrocarbyl, aryl or substituted aryl groups. The term "alkyl" also includes alkynyl groups containing at least one carbon-carbon triple bond, including straight-chain, branched-chain, and cyclic groups. Preferably, the

alkynyl group has about 2 to 12 carbons. More preferably it is a lower alkynyl of from about 2 to 7 carbons, more preferably about 2 to 4 carbons. The alkynyl group can be substituted or unsubstituted. When substituted the substituted group(s) preferably comprise hydroxy, oxy, thio, amino, nitro, cyano, alkoxy, alkyl-thio, alkyl-thio-alkyl, alkoxyalkyl, alkylamino, silyl, alkenyl, alkynyl, alkoxy, cycloalkenyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, C1-C6 hydrocarbonyl, aryl or substituted aryl groups. Alkyl groups or moieties of the invention can also include aryl, alkylaryl, carbocyclic aryl, heterocyclic aryl, amide and ester groups. The preferred substituent(s) of aryl groups are halogen, trihalomethyl, hydroxyl, SH, OH, cyano, alkoxy, alkyl, alkenyl, alkynyl, and amino groups. An "alkylaryl" group refers to an alkyl group (as described above) covalently joined to an aryl group (as described above). Carbocyclic aryl groups are groups wherein the ring atoms on the aromatic ring are all carbon atoms. The carbon atoms are optionally substituted. Heterocyclic aryl groups are groups having from about 1 to 3 heteroatoms as ring atoms in the aromatic ring and the remainder of the ring atoms are carbon atoms. Suitable heteroatoms include oxygen, sulfur, and nitrogen, and include furanyl, thienyl, pyridyl, pyrrolyl, N-lower alkyl pyrrolo, pyrimidyl, pyrazinyl, imidazolyl and the like, all optionally substituted. An "amide" refers to an -C(O)-NH-R, where R is either alkyl, aryl, alkylaryl or hydrogen. An "ester" refers to an -C(O)-OR', where R is either alkyl, aryl, alkylaryl or hydrogen.

The term "alkoxyalkyl" as used herein refers to an alkyl-O-alkyl ether, for example methoxyethyl or ethoxymethyl.

The term "alkyl-thio-alkyl" as used herein refers to an alkyl-S-alkyl thioether, for example methylthiomethyl or methylthioethyl.

The term "amination" as used herein refers to a process in which an amino group or substituted amine is introduced into an organic molecule.

The term "exocyclic amine protecting moiety" as used herein refers to a nucleobase amino protecting group compatible with oligonucleotide synthesis, for example an acyl or amide group.

The term "alkenyl" as used herein refers to a straight or branched hydrocarbon of a designed number of carbon atoms containing at least one carbon-carbon double bond. Examples of "alkenyl" include vinyl, allyl, and 2-methyl-3-heptene.

The term "alkoxy" as used herein refers to an alkyl group of indicated number of carbon atoms attached to the parent molecular moiety through an oxygen bridge. Examples of alkoxy groups include, for example, methoxy, ethoxy, propoxy and isopropoxy.

The term "alkynyl" as used herein refers to a straight or branched hydrocarbon of a designed number of carbon atoms containing at least one carbon-carbon triple bond. Examples of "alkynyl" include propargyl, propyne, and 3-hexyne.

5 The term "aryl" as used herein refers to an aromatic hydrocarbon ring system containing at least one aromatic ring. The aromatic ring can optionally be fused or otherwise attached to other aromatic hydrocarbon rings or non-aromatic hydrocarbon rings. Examples of aryl groups include, for example, phenyl, naphthyl, 1,2,3,4-tetrahydronaphthalene and biphenyl. Preferred examples of aryl groups include phenyl and naphthyl.

10 The term "cycloalkenyl" as used herein refers to a C3-C8 cyclic hydrocarbon containing at least one carbon-carbon double bond. Examples of cycloalkenyl include cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclopentadiene, cyclohexenyl, 1,3-cyclohexadiene, cycloheptenyl, cycloheptatrienyl, and cyclooctenyl.

15 The term "cycloalkyl" as used herein refers to a C3-C8 cyclic hydrocarbon. Examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl.

The term "cycloalkylalkyl," as used herein, refers to a C3-C7 cycloalkyl group attached to the parent molecular moiety through an alkyl group, as defined above. Examples of cycloalkylalkyl groups include cyclopropylmethyl and cyclopentylethyl.

20 The terms "halogen" or "halo" as used herein refers to indicate fluorine, chlorine, bromine, and iodine.

25 The term "heterocycloalkyl," as used herein refers to a non-aromatic ring system containing at least one heteroatom selected from nitrogen, oxygen, and sulfur. The heterocycloalkyl ring can be optionally fused to or otherwise attached to other heterocycloalkyl rings and/or non-aromatic hydrocarbon rings. Preferred heterocycloalkyl groups have from 3 to 7 members. Examples of heterocycloalkyl groups include, for example, piperazine, morpholine, piperidine, tetrahydrofuran, pyrrolidine, and pyrazole. Preferred heterocycloalkyl groups include piperidinyl, piperazinyl, morpholinyl, and pyrrolidinyl.

30 The term "heteroaryl" as used herein refers to an aromatic ring system containing at least one heteroatom selected from nitrogen, oxygen, and sulfur. The heteroaryl ring can be fused or otherwise attached to one or more heteroaryl rings, aromatic or non-aromatic hydrocarbon rings or heterocycloalkyl rings. Examples of heteroaryl groups include, for example, pyridine, furan, thiophene, 5,6,7,8-tetrahydroisoquinoline and pyrimidine. Preferred examples of heteroaryl groups include thienyl, benzothienyl, pyridyl, quinolyl,

pyrazinyl, pyrimidyl, imidazolyl, benzimidazolyl, furanyl, benzofuranyl, thiazolyl, benzothiazolyl, isoxazolyl, oxadiazolyl, isothiazolyl, benzisothiazolyl, triazolyl, tetrazolyl, pyrrolyl, indolyl, pyrazolyl, and benzopyrazolyl.

The term "C1-C6 hydrocarbyl" as used herein refers to straight, branched, or cyclic alkyl groups having 1-6 carbon atoms, optionally containing one or more carbon-carbon double or triple bonds. Examples of hydrocarbyl groups include, for example, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, pentyl, 2-pentyl, isopentyl, neopentyl, hexyl, 2-hexyl, 3-hexyl, 3-methylpentyl, vinyl, 2-pentene, cyclopropylmethyl, cyclopropyl, cyclohexylmethyl, cyclohexyl and propargyl. When reference is made herein to C1-C6 hydrocarbyl containing one or two double or triple bonds it is understood that at least two carbons are present in the alkyl for one double or triple bond, and at least four carbons for two double or triple bonds.

The term "nucleotide" as used herein refers to a heterocyclic nitrogenous base in N-glycosidic linkage with a phosphorylated sugar. Nucleotides are recognized in the art to include natural bases (standard), and modified bases well known in the art. Such bases are generally located at the 1' position of a nucleotide sugar moiety. Nucleotides generally comprise a base, sugar and a phosphate group. The nucleotides can be unmodified or modified at the sugar, phosphate and/or base moiety, (also referred to interchangeably as nucleotide analogs, modified nucleotides, non-natural nucleotides, non-standard nucleotides and other; see for example, Usman and McSwiggen, *supra*; Eckstein *et al.*, International PCT Publication No. WO 92/07065; Usman *et al.*, International PCT Publication No. WO 93/15187; Uhlman & Peyman, *supra* all are hereby incorporated by reference herein. There are several examples of modified nucleic acid bases known in the art as summarized by Limbach *et al.*, 1994, Nucleic Acids Res. 22, 2183. Some of the non-limiting examples of chemically modified and other natural nucleic acid bases that can be introduced into nucleic acids include, for example, inosine, purine, pyridin-4-one, pyridin-2-one, phenyl, pseudouracil, 2, 4, 6-trimethoxy benzene, 3-methyl uracil, dihydrouridine, naphthyl, aminophenyl, 5-alkylcytidines (*e.g.*, 5-methylcytidine), 5-alkyluridines (*e.g.*, ribothymidine), 5-halouridine (*e.g.*, 5-bromouridine) or 6-azapyrimidines or 6-alkylpyrimidines (*e.g.* 6-methyluridine), propyne, quesosine, 2-thiouridine, 4-thiouridine, wybutosine, wybutoxosine, 4-acetylcytidine, 5-(carboxyhydroxymethyl)uridine, 5'-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluridine, beta-D-galactosylqueosine, 1-methyladenosine, 1-methylinosine, 2,2-dimethylguanosine, 3-methylcytidine, 2-methyladenosine, 2-methylguanosine, N6-methyladenosine, 7-methylguanosine, 5-methoxyaminomethyl-2-thiouridine, 5-methylaminomethyluridine, 5-methylcarbonylmethyluridine, 5-methoxyuridine, 5-methyl-2-thiouridine, 2-methylthio-N6-isopentenyladenosine, beta-D-mannosylqueosine, uridine-5-oxyacetic acid, 2-thiocytidine,

threonine derivatives and others (Burgin *et al.*, 1996, Biochemistry, 35, 14090; Uhlman & Peyman, *supra*). By "modified bases" in this aspect is meant nucleotide bases other than adenine, guanine, cytosine and uracil at 1' position or their equivalents; such bases can be used at any position, for example, within the catalytic core of an enzymatic nucleic acid molecule and/or in the substrate-binding regions of the nucleic acid molecule.

The term "nucleoside" as used herein refers to a heterocyclic nitrogenous base in N-glycosidic linkage with a sugar. Nucleosides are recognized in the art to include natural bases (standard), and modified bases well known in the art. Such bases are generally located at the 1' position of a nucleoside sugar moiety. Nucleosides generally comprise a base and sugar group. The nucleosides can be unmodified or modified at the sugar, and/or base moiety (also referred to interchangeably as nucleoside analogs, modified nucleosides, non-natural nucleosides, non-standard nucleosides and other; see for example, Usman and McSwiggen, *supra*; Eckstein *et al.*, International PCT Publication No. WO 92/07065; Usman *et al.*, International PCT Publication No. WO 93/15187; Uhlman & Peyman, *supra* all are hereby incorporated by reference herein). There are several examples of modified nucleic acid bases known in the art as summarized by Limbach *et al.*, 1994, Nucleic Acids Res. 22, 2183. Some of the non-limiting examples of chemically modified and other natural nucleic acid bases that can be introduced into nucleic acids include, inosine, purine, pyridin-4-one, pyridin-2-one, phenyl, pseudouracil, 2, 4, 6-trimethoxy benzene, 3-methyl uracil, dihydrouridine, naphthyl, aminophenyl, 5-alkylcytidines (*e.g.*, 5-methylcytidine), 5-alkyluridines (*e.g.*, ribothymidine), 5-halouridine (*e.g.*, 5-bromouridine) or 6-azapyrimidines or 6-alkylpyrimidines (*e.g.* 6-methyluridine), propyne, quesosine, 2-thiouridine, 4-thiouridine, wybutosine, wybutoxosine, 4-acetylcytidine, 5-(carboxyhydroxymethyl)uridine, 5'-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluridine, beta-D-galactosylqueosine, 1-methyladenosine, 1-methylinosine, 2,2-dimethylguanosine, 3-methylcytidine, 2-methyladenosine, 2-methylguanosine, N6-methyladenosine, 7-methylguanosine, 5-methoxyaminomethyl-2-thiouridine, 5-methylaminomethyluridine, 5-methylcarbonylmethyluridine, 5-methoxyuridine, 5-methyl-2-thiouridine, 2-methylthio-N6-isopentenyladenosine, beta-D-mannosylqueosine, uridine-5-oxyacetic acid, 2-thiocytidine, threonine derivatives and others (Burgin *et al.*, 1996, Biochemistry, 35, 14090; Uhlman & Peyman, *supra*). By "modified bases" in this aspect is meant nucleoside bases other than adenine, guanine, cytosine and uracil at 1' position or their equivalents; such bases can be used at any position, for example, within the catalytic core of an enzymatic nucleic acid molecule and/or in the substrate-binding regions of the nucleic acid molecule.

In one embodiment, the invention features modified nucleic acid molecules with phosphate backbone modifications comprising one or more phosphorothioate, phosphorodithioate, methylphosphonate, morpholino, amidate carbamate, carboxymethyl,

acetamidate, polyamide, sulfonate, sulfonamide, sulfamate, formacetal, thioformacetal, and/or alkylsilyl, substitutions. For a review of oligonucleotide backbone modifications see Hunziker and Leumann, 1995, *Nucleic Acid Analogues: Synthesis and Properties*, in *Modern Synthetic Methods*, VCH, 331-417, and Mesmaeker *et al.*, 1994, *Novel Backbone Replacements for Oligonucleotides*, in *Carbohydrate Modifications in Antisense Research*, ACS, 24-39. These references are hereby incorporated by reference herein.

The term "abasic" as used herein refers to sugar moieties lacking a base or having other chemical groups in place of a base at the 1' position, for example a 3',3'-linked or 5',5'-linked deoxyabasic ribose derivative (for more details see Wincott *et al.*, International PCT publication No. WO 97/26270).

The term "unmodified nucleoside" as used herein refers to one of the bases adenine, cytosine, guanine, thymine, uracil joined to the 1' carbon of β -D-ribo-furanose.

The term "modified nucleoside" as used herein refers to any nucleotide base which contains a modification in the chemical structure of an unmodified nucleotide base, sugar and/or phosphate.

In connection with 2'-modified nucleotides as described for the present invention, by "amino" is meant 2'-NH₂ or 2'-O- NH₂, which can be modified or unmodified. Such modified groups are described, for example, in Eckstein *et al.*, U.S. Patent 5,672,695 and Matulic-Adamic *et al.*, WO 98/28317, respectively, which are both incorporated by reference in their entireties.

Various modifications to nucleic acid (*e.g.*, enzymatic nucleic acid, antisense, decoy, aptamer, siRNA, triplex oligonucleotides, 2,5-A oligonucleotides and other nucleic acid molecules) structure can be made to enhance the utility of these molecules. For example, such modifications can enhance shelf life, half-life *in vitro*, stability, and ease of introduction of such oligonucleotides to the target site, including *e.g.*, enhancing penetration of cellular membranes and conferring the ability to recognize and bind to targeted cells.

Use of these molecules can lead to better treatment of the disease progression by affording the possibility of combination therapies (*e.g.*, multiple nucleic acid molecules targeted to different genes, nucleic acid molecules coupled with known small molecule inhibitors, or intermittent treatment with combinations of nucleic acid molecules (including different nucleic acid molecule motifs) and/or other chemical or biological molecules). The treatment of patients with nucleic acid molecules can also include combinations of different types of nucleic acid molecules. Therapies can be devised which include a mixture of enzymatic nucleic acid molecules (including different enzymatic nucleic acid molecule

motifs), antisense, decoy, aptamer and/or 2-5A chimera molecules to one or more targets to alleviate symptoms of a disease.

Administration of Nucleic Acid Molecules

Methods for the delivery of nucleic acid molecules are described in Akhtar *et al.*, 1992, *Trends Cell Bio.*, 2, 139; *Delivery Strategies for Antisense Oligonucleotide Therapeutics*, ed. Akhtar, 1995, Maurer *et al.*, 1999, *Mol. Membr. Biol.*, 16, 129-140; Hofland and Huang, 1999, *Handb. Exp. Pharmacol.*, 137, 165-192; and Lee *et al.*, 2000, *ACS Symp. Ser.*, 752, 184-192, Sullivan *et al.*, PCT WO 94/02595, further describes the general methods for delivery of enzymatic nucleic acid molecules. These protocols can be utilized for the delivery of virtually any nucleic acid molecule. Nucleic acid molecules can be administered to cells by a variety of methods known to those of skill in the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres, or by proteinaceous vectors (O'Hare and Normand, International PCT Publication No. WO 00/53722). Alternatively, the nucleic acid/vehicle combination is locally delivered by direct injection or by use of an infusion pump. Direct injection of the nucleic acid molecules of the invention, whether subcutaneous, intramuscular, or intradermal, can take place using standard needle and syringe methodologies, or by needle-free technologies such as those described in Conry *et al.*, 1999, *Clin. Cancer Res.*, 5, 2330-2337 and Barry *et al.*, International PCT Publication No. WO 99/31262. The molecules of the instant invention can be used as pharmaceutical agents. Pharmaceutical agents prevent, modulate the occurrence, or treat (alleviate a symptom to some extent, preferably all of the symptoms) of a disease state in a patient.

Thus, the invention features a pharmaceutical composition comprising one or more nucleic acid(s) of the invention in an acceptable carrier, such as a stabilizer, buffer, and the like. The negatively charged polynucleotides of the invention can be administered (*e.g.*, RNA, DNA or protein) and introduced into a patient by any standard means, with or without stabilizers, buffers, and the like, to form a pharmaceutical composition. When it is desired to use a liposome delivery mechanism, standard protocols for formation of liposomes can be followed. The compositions of the present invention may also be formulated and used as tablets, capsules or elixirs for oral administration, suppositories for rectal administration, sterile solutions, suspensions for injectable administration, and the other compositions known in the art.

The present invention also includes pharmaceutically acceptable formulations of the compounds described. These formulations include salts of the above compounds, *e.g.*, acid

addition salts, for example, salts of hydrochloric, hydrobromic, acetic acid, and benzene sulfonic acid.

A pharmacological composition or formulation refers to a composition or formulation in a form suitable for administration, *e.g.*, systemic administration, into a cell or patient, including for example a human. Suitable forms, in part, depend upon the use or the route of entry, for example oral, transdermal, or by injection. Such forms should not prevent the composition or formulation from reaching a target cell (*i.e.*, a cell to which the negatively charged nucleic acid is desirable for delivery). For example, pharmacological compositions injected into the blood stream should be soluble. Other factors are known in the art, and include considerations such as toxicity and forms that prevent the composition or formulation from exerting its effect.

By “systemic administration” is meant *in vivo* systemic absorption or accumulation of drugs in the blood stream followed by distribution throughout the entire body. Administration routes which lead to systemic absorption include, without limitation: intravenous, subcutaneous, intraperitoneal, inhalation, oral, intrapulmonary and intramuscular. Each of these administration routes expose the desired negatively charged polymers, *e.g.*, nucleic acids, to an accessible diseased tissue. The rate of entry of a drug into the circulation has been shown to be a function of molecular weight or size. The use of a liposome or other drug carrier comprising the compounds of the instant invention can potentially localize the drug, for example, in certain tissue types, such as the tissues of the reticular endothelial system (RES). A liposome formulation that can facilitate the association of drug with the surface of cells, such as, lymphocytes and macrophages is also useful. This approach may provide enhanced delivery of the drug to target cells by taking advantage of the specificity of macrophage and lymphocyte immune recognition of abnormal cells, such as cancer cells.

By “pharmaceutically acceptable formulation” is meant, a composition or formulation that allows for the effective distribution of the nucleic acid molecules of the instant invention in the physical location most suitable for their desired activity. Nonlimiting examples of agents suitable for formulation with the nucleic acid molecules of the instant invention include: P-glycoprotein inhibitors (such as Pluronic P85), which can enhance entry of drugs into the CNS (Jolliet-Riant and Tillement, 1999, *Fundam. Clin. Pharmacol.*, 13, 16-26); biodegradable polymers, such as poly (DL-lactide-coglycolide) microspheres for sustained release delivery after intracerebral implantation (Emerich, DF *et al*, 1999, *Cell Transplant*, 8, 47-58) (Alkermes, Inc. Cambridge, MA); and loaded nanoparticles, such as those made of polybutylcyanoacrylate, which can deliver drugs across the blood brain barrier and can alter neuronal uptake mechanisms (*Prog Neuropsychopharmacol Biol Psychiatry*, 23, 941-949,

1999). Other non-limiting examples of delivery strategies for the nucleic acid molecules of the instant invention include material described in Boado *et al.*, 1998, *J. Pharm. Sci.*, 87, 1308-1315; Tyler *et al.*, 1999, *FEBS Lett.*, 421, 280-284; Pardridge *et al.*, 1995, *PNAS USA*, 92, 5592-5596; Boado, 1995, *Adv. Drug Delivery Rev.*, 15, 73-107; Aldrian-Herrada *et al.*,
 5 1998, *Nucleic Acids Res.*, 26, 4910-4916; and Tyler *et al.*, 1999, *PNAS USA*, 96, 7053-7058.

The invention also features the use of the composition comprising surface-modified liposomes containing poly (ethylene glycol) lipids (PEG-modified, or long-circulating liposomes or stealth liposomes). These formulations offer a method for increasing the accumulation of drugs in target tissues. This class of drug carriers resists opsonization and
 10 elimination by the mononuclear phagocytic system (MPS or RES), thereby enabling longer blood circulation times and enhanced tissue exposure for the encapsulated drug (Lasic *et al. Chem. Rev.* 1995, 95, 2601-2627; Ishiwata *et al.*, *Chem. Pharm. Bull.* 1995, 43, 1005-1011). Such liposomes have been shown to accumulate selectively in tumors, presumably by extravasation and capture in the neovascularized target tissues (Lasic *et al.*, *Science* 1995,
 15 267, 1275-1276; Oku *et al.*, 1995, *Biochim. Biophys. Acta*, 1238, 86-90). The long-circulating liposomes enhance the pharmacokinetics and pharmacodynamics of DNA and RNA, particularly compared to conventional cationic liposomes which are known to accumulate in tissues of the MPS (Liu *et al.*, *J. Biol. Chem.* 1995, 270, 24864-24870; Choi *et al.*, International PCT Publication No. WO 96/10391; Ansell *et al.*, International PCT Publication
 20 No. WO 96/10390; Holland *et al.*, International PCT Publication No. WO 96/10392). Long-circulating liposomes are also likely to protect drugs from nuclease degradation to a greater extent compared to cationic liposomes, based on their ability to avoid accumulation in metabolically aggressive MPS tissues such as the liver and spleen.

The present invention also includes compositions prepared for storage or
 25 administration, which include a pharmaceutically effective amount of the desired compounds in a pharmaceutically acceptable carrier or diluent. Acceptable carriers or diluents for therapeutic use are well known in the pharmaceutical art, and are described, for example, in *Remington's Pharmaceutical Sciences*, Mack Publishing Co. (A.R. Gennaro edit. 1985) hereby incorporated by reference herein. For example, preservatives, stabilizers, dyes and
 30 flavoring agents may be provided. These include sodium benzoate, sorbic acid and esters of *p*-hydroxybenzoic acid. In addition, antioxidants and suspending agents may be used.

A pharmaceutically effective dose is that dose required to prevent, inhibit the occurrence of, or treat (alleviate a symptom to some extent, preferably all of the symptoms) a disease state. The pharmaceutically effective dose depends on the type of disease, the
 35 composition used, the route of administration, the type of mammal being treated, the physical characteristics of the specific mammal under consideration, concurrent medication, and other

factors that those skilled in the medical arts will recognize. Generally, an amount between 0.1 mg/kg and 100 mg/kg body weight/day of active ingredients is administered dependent upon potency of the negatively charged polymer.

5 The present invention also includes compositions prepared for storage or administration that include a pharmaceutically effective amount of the desired compounds in a pharmaceutically acceptable carrier or diluent. Acceptable carriers or diluents for therapeutic use are well known in the pharmaceutical art, and are described, for example, in *Remington's Pharmaceutical Sciences*, Mack Publishing Co. (A.R. Gennaro edit. 1985), hereby incorporated by reference herein. For example, preservatives, stabilizers, dyes and flavoring agents can be provided. These include sodium benzoate, sorbic acid and esters of *p*-hydroxybenzoic acid. In addition, antioxidants and suspending agents can be used.

15 A pharmaceutically effective dose is that dose required to prevent, inhibit the occurrence, or treat (alleviate a symptom to some extent, preferably all of the symptoms) of a disease state. The pharmaceutically effective dose depends on the type of disease, the composition used, the route of administration, the type of mammal being treated, the physical characteristics of the specific mammal under consideration, concurrent medication, and other factors that those skilled in the medical arts will recognize. Generally, an amount between 0.1 mg/kg and 100 mg/kg body weight/day of active ingredients is administered dependent upon potency of the negatively charged polymer.

20 The nucleic acid molecules of the invention and formulations thereof can be administered orally, topically, parenterally, by inhalation or spray, or rectally in dosage unit formulations containing conventional non-toxic pharmaceutically acceptable carriers, adjuvants and/or vehicles. The term parenteral as used herein includes percutaneous, subcutaneous, intravascular (*e.g.*, intravenous), intramuscular, or intrathecal injection or infusion techniques and the like. In addition, there is provided a pharmaceutical formulation comprising a nucleic acid molecule of the invention and a pharmaceutically acceptable carrier. One or more nucleic acid molecules of the invention can be present in association with one or more non-toxic pharmaceutically acceptable carriers and/or diluents and/or adjuvants, and if desired other active ingredients. The pharmaceutical compositions containing nucleic acid molecules of the invention can be in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsion, hard or soft capsules, or syrups or elixirs.

35 Compositions intended for oral use can be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions can contain one or more such sweetening agents, flavoring agents, coloring agents or preservative agents in order to provide pharmaceutically elegant and palatable preparations. Tablets

contain the active ingredient in admixture with non-toxic pharmaceutically acceptable excipients that are suitable for the manufacture of tablets. These excipients can be, for example, inert diluents; such as calcium carbonate, sodium carbonate, lactose, calcium phosphate or sodium phosphate; granulating and disintegrating agents, for example, corn starch, or alginic acid; binding agents, for example starch, gelatin or acacia; and lubricating agents, for example magnesium stearate, stearic acid or talc. The tablets can be uncoated or they can be coated by known techniques. In some cases such coatings can be prepared by known techniques to delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate can be employed.

Formulations for oral use can also be presented as hard gelatin capsules wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water or an oil medium, for example peanut oil, liquid paraffin or olive oil.

Aqueous suspensions contain the active materials in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients are suspending agents, for example sodium carboxymethylcellulose, methylcellulose, hydropropyl-methylcellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents can be a naturally-occurring phosphatide, for example, lecithin, or condensation products of an alkylene oxide with fatty acids, for example polyoxyethylene stearate, or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethyleneoxycetanol, or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan monooleate. The aqueous suspensions can also contain one or more preservatives, for example ethyl, or n-propyl p-hydroxybenzoate, one or more coloring agents, one or more flavoring agents, and one or more sweetening agents, such as sucrose or saccharin.

Oily suspensions can be formulated by suspending the active ingredients in a vegetable oil, for example arachis oil, olive oil, sesame oil or coconut oil, or in a mineral oil such as liquid paraffin. The oily suspensions can contain a thickening agent, for example beeswax, hard paraffin or cetyl alcohol. Sweetening agents and flavoring agents can be added to provide palatable oral preparations. These compositions can be preserved by the addition of an anti-oxidant such as ascorbic acid.

Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in admixture with a dispersing or wetting

agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents or suspending agents are exemplified by those already mentioned above. Additional excipients, for example sweetening, flavoring and coloring agents, can also be present.

5 Pharmaceutical compositions of the invention can also be in the form of oil-in-water emulsions. The oily phase can be a vegetable oil or a mineral oil or mixtures of these. Suitable emulsifying agents can be naturally-occurring gums, for example gum acacia or gum tragacanth, naturally-occurring phosphatides, for example soy bean, lecithin, and esters or partial esters derived from fatty acids and hexitol, anhydrides, for example sorbitan monooleate, and condensation products of the said partial esters with ethylene oxide, for
10 example polyoxyethylene sorbitan monooleate. The emulsions can also contain sweetening and flavoring agents.

 Syrups and elixirs can be formulated with sweetening agents, for example glycerol, propylene glycol, sorbitol, glucose or sucrose. Such formulations can also contain a demulcent, a preservative and flavoring and coloring agents. The pharmaceutical
15 compositions can be in the form of a sterile injectable aqueous or oleaginous suspension. This suspension can be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents that have been mentioned above. The sterile injectable preparation can also be a sterile injectable solution or suspension in a non-toxic parentally acceptable diluent or solvent, for example as a solution in 1,3-butanediol. Among
20 the acceptable vehicles and solvents that can be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose, any bland fixed oil can be employed including synthetic mono-or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

25 The nucleic acid molecules of the invention can also be administered in the form of suppositories, *e.g.*, for rectal administration of the drug. These compositions can be prepared by mixing the drug with a suitable non-irritating excipient that is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum to release the drug. Such materials include cocoa butter and polyethylene glycols.

30 Nucleic acid molecules of the invention can be administered parenterally in a sterile medium. The drug, depending on the vehicle and concentration used, can either be suspended or dissolved in the vehicle. Advantageously, adjuvants such as local anesthetics, preservatives and buffering agents can be dissolved in the vehicle.

35 Dosage levels of the order of from about 0.1 mg to about 140 mg per kilogram of body weight per day are useful in the treatment of the above-indicated conditions (about 0.5 mg to

about 7 g per patient per day). The amount of active ingredient that can be combined with the carrier materials to produce a single dosage form varies depending upon the host treated and the particular mode of administration. Dosage unit forms generally contain between from about 1 mg to about 500 mg of an active ingredient.

5 It is understood that the specific dose level for any particular patient depends upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of administration, route of administration, and rate of excretion, drug combination and the severity of the particular disease undergoing therapy.

10 For administration to non-human animals, the composition can also be added to the animal feed or drinking water. It can be convenient to formulate the animal feed and drinking water compositions so that the animal takes in a therapeutically appropriate quantity of the composition along with its diet. It can also be convenient to present the composition as a premix for addition to the feed or drinking water.

15 The nucleic acid molecules of the present invention may also be administered to a patient in combination with other therapeutic compounds to increase the overall therapeutic effect. The use of multiple compounds to treat an indication may increase the beneficial effects while reducing the presence of side effects.

20 In one embodiment, the invention compositions suitable for administering nucleic acid molecules of the invention to specific cell types, such as hepatocytes. For example, the asialoglycoprotein receptor (ASGPr) (Wu and Wu, 1987, *J. Biol. Chem.* 262, 4429-4432) is unique to hepatocytes and binds branched galactose-terminal glycoproteins, such as asialoorosomucoid (ASOR). Binding of such glycoproteins or synthetic glycoconjugates to the receptor takes place with an affinity that strongly depends on the degree of branching of the oligosaccharide chain, for example, triantennary structures are bound with greater affinity
25 than biantennary or monoantennary chains (Baenziger and Fiete, 1980, *Cell*, 22, 611-620; Connolly *et al.*, 1982, *J. Biol. Chem.*, 257, 939-945). Lee and Lee, 1987, *Glycoconjugate J.*, 4, 317-328, obtained this high specificity through the use of N-acetyl-D-galactosamine as the carbohydrate moiety, which has higher affinity for the receptor, compared to galactose. This "clustering effect" has also been described for the binding and uptake of mannosyl-
30 terminating glycoproteins or glycoconjugates (Ponpipom *et al.*, 1981, *J. Med. Chem.*, 24, 1388-1395). The use of galactose and galactosamine based conjugates to transport exogenous compounds across cell membranes can provide a targeted delivery approach to the treatment of liver disease such as HBV infection or hepatocellular carcinoma. The use of bioconjugates can also provide a reduction in the required dose of therapeutic compounds required for
35 treatment. Furthermore, therapeutic bioavailability, pharmacodynamics, and pharmacokinetic parameters can be modulated through the use of nucleic acid bioconjugates of the invention.

Alternatively, certain of the nucleic acid molecules of the instant invention can be expressed within cells from eukaryotic promoters (e.g., Izant and Weintraub, 1985, *Science*, 229, 345; McGarry and Lindquist, 1986, *Proc. Natl. Acad. Sci.*, USA 83, 399; Scanlon *et al.*, 1991, *Proc. Natl. Acad. Sci. USA*, 88, 10591-5; Kashani-Sabet *et al.*, 1992, *Antisense Res. Dev.*, 2, 3-15; Dropulic *et al.*, 1992, *J. Virol.*, 66, 1432-41; Weerasinghe *et al.*, 1991, *J. Virol.*, 65, 5531-4; Ojwang *et al.*, 1992, *Proc. Natl. Acad. Sci. USA*, 89, 10802-6; Chen *et al.*, 1992, *Nucleic Acids Res.*, 20, 4581-9; Sarver *et al.*, 1990 *Science*, 247, 1222-1225; Thompson *et al.*, 1995, *Nucleic Acids Res.*, 23, 2259; Good *et al.*, 1997, *Gene Therapy*, 4, 45; all of these references are hereby incorporated in their totalities by reference herein). Those skilled in the art realize that any nucleic acid can be expressed in eukaryotic cells from the appropriate DNA/RNA vector. The activity of such nucleic acids can be augmented by their release from the primary transcript by a ribozyme (Draper *et al.*, PCT WO 93/23569, and Sullivan *et al.*, PCT WO 94/02595; Ohkawa *et al.*, 1992, *Nucleic Acids Symp. Ser.*, 27, 15-6; Taira *et al.*, 1991, *Nucleic Acids Res.*, 19, 5125-30; Ventura *et al.*, 1993, *Nucleic Acids Res.*, 21, 3249-55; Chowrira *et al.*, 1994, *J. Biol. Chem.*, 269, 25856; all of these references are hereby incorporated in their totality by reference herein).

In another aspect of the invention, RNA molecules of the present invention are preferably expressed from transcription units (see, for example, Couture *et al.*, 1996, *TIG.*, 12, 510) inserted into DNA or RNA vectors. The recombinant vectors are preferably DNA plasmids or viral vectors. Ribozyme expressing viral vectors could be constructed based on, but not limited to, adeno-associated virus, retrovirus, adenovirus, or alphavirus. Preferably, the recombinant vectors capable of expressing the nucleic acid molecules are delivered as described above, and persist in target cells. Alternatively, viral vectors may be used that provide for transient expression of nucleic acid molecules. Such vectors might be repeatedly administered as necessary. Once expressed, the nucleic acid molecule binds to the target mRNA. Delivery of nucleic acid molecule expressing vectors could be systemic, such as by intravenous or intra-muscular administration, by administration to target cells ex-planted from the patient followed by reintroduction into the patient, or by any other means that would allow for introduction into the desired target cell (for a review see Couture *et al.*, 1996, *TIG.*, 12, 510).

In one aspect, the invention features an expression vector comprising a nucleic acid sequence encoding at least one of the nucleic acid molecules of the instant invention is disclosed. The nucleic acid sequence encoding the nucleic acid molecule of the instant invention is operable linked in a manner which allows expression of that nucleic acid molecule.

In another aspect the invention features an expression vector comprising: a) a transcription initiation region (*e.g.*, eukaryotic pol I, II or III initiation region); b) a transcription termination region (*e.g.*, eukaryotic pol I, II or III termination region); c) a nucleic acid sequence encoding at least one of the nucleic acid catalyst of the instant invention; and wherein said sequence is operably linked to said initiation region and said termination region, in a manner which allows expression and/or delivery of said nucleic acid molecule. The vector may optionally include an open reading frame (ORF) for a protein operably linked on the 5' side or the 3'-side of the sequence encoding the nucleic acid catalyst of the invention; and/or an intron (intervening sequences).

Transcription of the nucleic acid molecule sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, etc.) present nearby. Prokaryotic RNA polymerase promoters are also used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells (Elroy-Stein and Moss, 1990, *Proc. Natl. Acad. Sci. U S A*, 87, 6743-7; Gao and Huang 1993, *Nucleic Acids Res.*, 21, 2867-72; Lieber et al., 1993, *Methods Enzymol.*, 217, 47-66; Zhou et al., 1990, *Mol. Cell. Biol.*, 10, 4529-37). All of these references are incorporated by reference herein. Several investigators have demonstrated that nucleic acid molecules, such as ribozymes expressed from such promoters can function in mammalian cells (*e.g.* Kashani-Sabet et al., 1992, *Antisense Res. Dev.*, 2, 3-15; Ojwang et al., 1992, *Proc. Natl. Acad. Sci. U S A*, 89, 10802-6; Chen et al., 1992, *Nucleic Acids Res.*, 20, 4581-9; Yu et al., 1993, *Proc. Natl. Acad. Sci. U S A*, 90, 6340-4; L'Huillier et al., 1992, *EMBO J.*, 11, 4411-8; Lisiewicz et al., 1993, *Proc. Natl. Acad. Sci. U. S. A*, 90, 8000-4; Thompson et al., 1995, *Nucleic Acids Res.*, 23, 2259; Sullenger & Cech, 1993, *Science*, 262, 1566). More specifically, transcription units such as the ones derived from genes encoding U6 small nuclear (snRNA), transfer RNA (tRNA) and adenovirus VA RNA are useful in generating high concentrations of desired RNA molecules such as ribozymes in cells (Thompson et al., *supra*; Couture and Stinchcomb, 1996, *supra*; Noonberg et al., 1994, *Nucleic Acid Res.*, 22, 2830; Noonberg et al., US Patent No. 5,624,803; Good et al., 1997, *Gene Ther.*, 4, 45; Beigelman et al., International PCT Publication No. WO 96/18736; all of these publications are incorporated by reference herein). The above ribozyme transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated virus vectors), or viral RNA vectors (such as retroviral or alphavirus vectors) (for a review see Couture and Stinchcomb, 1996, *supra*).

In yet another aspect, the invention features an expression vector comprising nucleic acid sequence encoding at least one of the nucleic acid molecules of the invention, in a manner that allows expression of that nucleic acid molecule. The expression vector comprises in one embodiment; a) a transcription initiation region; b) a transcription termination region; c) a nucleic acid sequence encoding at least one said nucleic acid molecule; and wherein said sequence is operably linked to said initiation region and said termination region, in a manner which allows expression and/or delivery of said nucleic acid molecule. In another embodiment, the expression vector comprises: a) a transcription initiation region; b) a transcription termination region; c) an open reading frame; d) a nucleic acid sequence encoding at least one said nucleic acid molecule, wherein said sequence is operably linked to the 3'-end of said open reading frame; and wherein said sequence is operably linked to said initiation region, said open reading frame and said termination region, in a manner which allows expression and/or delivery of said nucleic acid molecule. In yet another embodiment, the expression vector comprises: a) a transcription initiation region; b) a transcription termination region; c) an intron; d) a nucleic acid sequence encoding at least one said nucleic acid molecule; and wherein said sequence is operably linked to said initiation region, said intron and said termination region, in a manner which allows expression and/or delivery of said nucleic acid molecule. In another embodiment, the expression vector comprises: a) a transcription initiation region; b) a transcription termination region; c) an intron; d) an open reading frame; e) a nucleic acid sequence encoding at least one said nucleic acid molecule, wherein said sequence is operably linked to the 3'-end of said open reading frame; and wherein said sequence is operably linked to said initiation region, said intron, said open reading frame and said termination region, in a manner which allows expression and/or delivery of said nucleic acid molecule.

Interferons

Type I interferons (IFN) are a class of natural cytokines that includes a family of greater than 25 IFN- α (Pesta, 1986, *Methods Enzymol.* 119, 3-14) as well as IFN- β , and IFN- ω . Although evolutionarily derived from the same gene (Diaz *et al.*, 1994, *Genomics* 22, 540-552), there are many differences in the primary sequence of these molecules, implying an evolutionary divergence in biologic activity. All type I IFN share a common pattern of biologic effects that begin with binding of the IFN to the cell surface receptor (Pfeffer & Strulovici, 1992, Transmembrane secondary messengers for IFN- α/β . In: *Interferon. Principles and Medical Applications.*, S. Baron, D.H. Coopenhaver, F. Dianzani, W.R. Fleischmann Jr., T.K. Hughes Jr., G.R. Kimpel, D.W. Niesel, G.J. Stanton, and S.K. Tying, eds. 151-160). Binding is followed by activation of tyrosine kinases, including the Janus tyrosine kinases and the STAT proteins, which leads to the production of several IFN-stimulated gene products (Johnson *et al.*, 1994, *Sci. Am.* 270, 68-75). The IFN-stimulated

gene products are responsible for the pleiotropic biologic effects of type I IFN, including antiviral, antiproliferative, and immunomodulatory effects, cytokine induction, and HLA class I and class II regulation (Pestka *et al.*, 1987, *Annu. Rev. Biochem* 56, 727). Examples of IFN-stimulated gene products include 2-5-oligoadenylate synthetase (2-5 OAS), β_2 -microglobulin, neopterin, p68 kinases, and the Mx protein (Chebath & Revel, 1992, The 2-5 A system: 2-5 A synthetase, isospecies and functions. In: *Interferon. Principles and Medical Applications*. S. Baron, D.H. Coopenhaver, F. Dianzani, W.R. Jr. Fleischmann, T.K. Jr Hughes, G.R. Kimpel, D.W. Niesel, G.J. Stanton, and S.K. Tying, eds., pp. 225-236; Samuel, 1992, The RNA-dependent P1/eIF-2 α protein kinase. In: *Interferon. Principles and Medical Applications*. S. Baron, D.H. Coopenhaver, F. Dianzani, W.R. Fleischmann Jr., T.K. Hughes Jr., G.R. Kimpel, D.W. Niesel, G.H. Stanton, and S.K. Tying, eds. 237-250; Horisberger, 1992, MX protein: function and Mechanism of Action. In: *Interferon. Principles and Medical Applications*. S. Baron, D.H. Coopenhaver, F. Dianzani, W.R. Fleischmann Jr., T.K. Hughes Jr., G.R. Kimpel, D.W. Niesel, G.H. Stanton, and S.K. Tying, eds. 215-224). Although all type I IFN have similar biologic effects, not all the activities are shared by each type I IFN, and, in many cases, the extent of activity varies quite substantially for each IFN subtype (Fish *et al.*, 1989, *J. Interferon Res.* 9, 97-114; Ozes *et al.*, 1992, *J. Interferon Res.* 12, 55-59). More specifically, investigations into the properties of different subtypes of IFN- α and molecular hybrids of IFN- α have shown differences in pharmacologic properties (Rubinstein, 1987, *J. Interferon Res.* 7, 545-551). These pharmacologic differences can arise from as few as three amino acid residue changes (Lee *et al.*, 1982, *Cancer Res.* 42, 1312-1316).

Eighty-five to 166 amino acids are conserved in the known IFN- α subtypes. Excluding the IFN- α pseudogenes, there are approximately 25 known distinct IFN- α subtypes. Pairwise comparisons of these nonallelic subtypes show primary sequence differences ranging from 2% to 23%. In addition to the naturally occurring IFNs, a non-natural recombinant type I interferon known as consensus interferon (CIFN) has been synthesized as a therapeutic compound (Tong *et al.*, 1997, *Hepatology* 26, 747-754).

Interferon is currently in use for at least 12 different indications including infectious and autoimmune diseases and cancer (Borden, 1992, *N. Engl. J. Med.* 326, 1491-1492). For autoimmune diseases IFN has been utilized for treatment of rheumatoid arthritis, multiple sclerosis, and Crohn's disease. For treatment of cancer IFN has been used alone or in combination with a number of different compounds. Specific types of cancers for which IFN has been used include squamous cell carcinomas, melanomas, hypernephromas, hemangiomas, hairy cell leukemia, and Kaposi's sarcoma. In the treatment of infectious diseases, IFNs increase the phagocytic activity of macrophages and cytotoxicity of lymphocytes and inhibits the propagation of cellular pathogens. Specific indications for

which IFN has been used as treatment include: hepatitis B, human papillomavirus types 6 and 11 (i.e. genital warts) (Leventhal *et al.*, 1991, *N Engl J Med* 325, 613-617), chronic granulomatous disease, and hepatitis C virus.

5 Numerous well controlled clinical trials using IFN-alpha in the treatment of chronic HCV infection have demonstrated that treatment three times a week results in lowering of serum ALT values in approximately 50% (range 40% to 70%) of patients by the end of 6 months of therapy (Davis *et al.*, 1989, *The new England Journal of Medicine* 321, 1501-1506; Marcellin *et al.*, 1991, *Hepatology* 13, 393-397; Tong *et al.*, 1997, *Hepatology* 26, 747-754; Tong *et al.*, *Hepatology* 26, 1640-1645). However, following cessation of interferon
10 treatment, approximately 50% of the responding patients relapsed, resulting in a "durable" response rate as assessed by normalization of serum ALT concentrations of approximately 20 to 25%. In addition, studies that have examined six months of type 1 interferon therapy using changes in HCV RNA values as a clinical endpoint have demonstrated that up to 35% of patients will have a loss of HCV RNA by the end of therapy (Tong *et al.*, 1997, *supra*).
15 However, as with the ALT endpoint, about 50% of the patients relapse six months following cessation of therapy resulting in a durable virologic response of only 12% (23). Studies that have examined 48 weeks of therapy have demonstrated that the sustained virological response is up to 25%.

Pegylated interferons, ie. interferons conjugated with polyethylene glycol (PEG), have
20 demonstrated improved characteristics over interferon. Advantages incurred by PEG conjugation can include an improved pharmacokinetic profile compared to interferons lacking PEG, thus imparting more convenient dosing regimes, improved tolerance, and improved antiviral efficacy. Such improvements have been demonstrated in clinical studies of both polyethylene glycol interferon alfa-2a (PEGASYS, Roche) and polyethylene glycol
25 interferon alfa-2b (VIRAIFERON PEG, PEG-INTRON, Enzon/Schering Plough).

Enzymatic nucleic acid molecules in combination with interferons and polyethylene glycol interferons have the potential to improve the effectiveness of treatment of HCV or any of the other indications discussed above. Enzymatic nucleic acid molecules targeting RNAs associated with diseases such as infectious diseases, autoimmune diseases, and cancer, can be
30 used individually or in combination with other therapies such as interferons and polyethylene glycol interferons and to achieve enhanced efficacy.

Examples:

The following are non-limiting examples showing the selection, isolation, synthesis and activity of nucleic acids of the instant invention. These examples demonstrate the selection
35 and design of Antisense, Hammerhead, DNAzyme, NCH, Amberzyme, Zinzyme or G-

Cleaver ribozyme molecules and binding/cleavage sites within HBV and HCV RNA. The following examples also demonstrate the selection and design of nucleic acid decoy molecules that target HBV reverse transcriptase. The following examples also demonstrate the use of enzymatic nucleic acid molecules that cleave HCV RNA. The methods described herein represent a scheme by which nucleic acid molecules can be derived that cleave other RNA targets required for HCV replication.

Example 1: Identification of Potential Target Sites in Human HBV RNA

The sequence of human HBV was screened for accessible sites using a computer-folding algorithm. Regions of the RNA that did not form secondary folding structures and contained potential ribozyme and/or antisense binding/cleavage sites were identified. The sequences of these cleavage sites are shown in **Tables IV - XI**.

Example 2: Selection of Enzymatic Nucleic Acid Cleavage Sites in Human HBV RNA

Ribozyme target sites were chosen by analyzing sequences of Human HBV (accession number: AF100308.1) and prioritizing the sites on the basis of folding. Ribozymes were designed that could bind each target and were individually analyzed by computer folding (Christoffersen *et al.*, 1994 *J. Mol. Struc. Theochem*, 311, 273; Jaeger *et al.*, 1989, *Proc. Natl. Acad. Sci. USA*, **86**, 7706) to assess whether the ribozyme sequences fold into the appropriate secondary structure. Those ribozymes with unfavorable intramolecular interactions between the binding arms and the catalytic core were eliminated from consideration. As noted herein, varying binding arm lengths can be chosen to optimize activity. Generally, at least 5 bases on each arm are able to bind to, or otherwise interact with, the target RNA.

Example 3: Chemical Synthesis and Purification of Ribozymes and Antisense for Efficient Cleavage and/or blocking of HBV RNA

Ribozymes and antisense constructs were designed to anneal to various sites in the RNA message. The binding arms of the ribozymes are complementary to the target site sequences described above, while the antisense constructs are fully complementary to the target site sequences described above. The ribozymes and antisense constructs were chemically synthesized. The method of synthesis used followed the procedure for normal RNA synthesis as described above and in Usman *et al.*, (1987 *J. Am. Chem. Soc.*, 109, 7845), Scaringe *et al.*, (1990 *Nucleic Acids Res.*, 18, 5433) and Wincott *et al.*, *supra*, and made use of common nucleic acid protecting and coupling groups, such as dimethoxytrityl at the 5'-end, and phosphoramidites at the 3'-end. The average stepwise coupling yields were typically >98%.

Ribozymes and antisense constructs were also synthesized from DNA templates using bacteriophage T7 RNA polymerase (Milligan and Uhlenbeck, 1989, *Methods Enzymol.* 180, 51). Ribozymes and antisense constructs were purified by gel electrophoresis using general methods or were purified by high pressure liquid chromatography (HPLC; see Wincott et al., *supra*; the totality of which is hereby incorporated herein by reference) and were resuspended in water. The sequences of the chemically synthesized ribozymes used in this study are shown below in **Table XI**.

Example 4: Ribozyme Cleavage of HBV RNA Target *in vitro*

Ribozymes targeted to the human HBV RNA are designed and synthesized as described above. These ribozymes can be tested for cleavage activity *in vitro*, for example using the following procedure. The target sequences and the nucleotide location within the HBV RNA are given in **Tables IV-XI**.

Cleavage Reactions: Full-length or partially full-length, internally-labeled target RNA for ribozyme cleavage assay is prepared by *in vitro* transcription in the presence of [α - 32 P] CTP, passed over a G 50 Sephadex® column by spin chromatography and used as substrate RNA without further purification. Alternately, substrates are 5'- 32 P-end labeled using T4 polynucleotide kinase enzyme. Assays are performed by pre-warming a 2X concentration of purified ribozyme in ribozyme cleavage buffer (50 mM Tris-HCl, pH 7.5 at 37°C, 10 mM MgCl₂) and the cleavage reaction was initiated by adding the 2X ribozyme mix to an equal volume of substrate RNA (maximum of 1-5 nM) that was also pre-warmed in cleavage buffer. As an initial screen, assays are carried out for 1 hour at 37°C using a final concentration of either 40 nM or 1 mM ribozyme, *i.e.*, ribozyme excess. The reaction is quenched by the addition of an equal volume of 95% formamide, 20 mM EDTA, 0.05% bromophenol blue and 0.05% xylene cyanol after which the sample is heated to 95°C for 2 minutes, quick chilled and loaded onto a denaturing polyacrylamide gel. Substrate RNA and the specific RNA cleavage products generated by ribozyme cleavage are visualized on an autoradiograph of the gel. The percentage of cleavage is determined by Phosphor Imager® quantitation of bands representing the intact substrate and the cleavage products.

Example 5: Transfection of HepG2 Cells with psHBV-1 and Ribozymes

The human hepatocellular carcinoma cell line Hep G2 was grown in Dulbecco's modified Eagle media supplemented with 10% fetal calf serum, 2 mM glutamine, 0.1 mM nonessential amino acids, 1 mM sodium pyruvate, 25 mM Hepes, 100 units penicillin, and 100 µg/ml streptomycin. To generate a replication competent cDNA, prior to transfection the HBV genomic sequences are excised from the bacterial plasmid sequence contained in the psHBV-1 vector (Those skilled in the art understand that other methods may be used to

generate a replication competent cDNA). This was done with an EcoRI and Hind III restriction digest. Following completion of the digest, a ligation was performed under dilute conditions (20 µg/ml) to favor intermolecular ligation. The total ligation mixture was then concentrated using Qiagen spin columns.

5 Secreted alkaline phosphatase (SEAP) was used to normalize the HBsAg levels to control for transfection variability. The pSEAP2-TK control vector was constructed by ligating a Bgl II-Hind III fragment of the pRL-TK vector (Promega), containing the herpes simplex virus thymidine kinase promoter region, into *Bgl* II/*Hind* III digested pSEAP2-Basic (Clontech). Hep G2 cells were plated (3×10^4 cells/well) in 96-well microtiter plates and
10 incubated overnight. A lipid/DNA/ribozyme complex was formed containing (at final concentrations) cationic lipid (15 µg/ml), prepared psHBV-1 (4.5 µg/ml), pSEAP2-TK (0.5 µg/ml), and ribozyme (100 µM). Following a 15 min. incubation at 37° C, the complexes were added to the plated Hep G2 cells. Media was removed from the cells 96 hr. post-transfection for HBsAg and SEAP analysis.

15 Transfection of the human hepatocellular carcinoma cell line, Hep G2, with replication competent HBV DNA results in the expression of HBV proteins and the production of virions. To investigate the potential use of ribozymes for the treatment of chronic HBV infection, a series of ribozymes that target the 3' terminus of the HBV genome have been synthesized. Ribozymes targeting this region have the potential to cleave all four major HBV
20 RNA transcripts as well as the potential to block the production of HBV DNA by cleavage of the pregenomic RNA. To test the efficacy of these HBV ribozymes, they were co-transfected with HBV genomic DNA into Hep G2 cells, and the subsequent levels of secreted HBV surface antigen (HBsAg) were analyzed by ELISA. To control for variability in transfection efficiency, a control vector which expresses secreted alkaline phosphatase (SEAP), was also
25 co-transfected. The efficacy of the HBV ribozymes was determined by comparing the ratio of HBsAg:SEAP and/or HBeAg:SEAP to that of a scrambled attenuated control (SAC) ribozyme. Twenty-five ribozymes (RPI18341, RPI18356, RPI18363, RPI18364, RPI18365, RPI18366, RPI18367, RPI18368, RPI18369, RPI18370, RPI18371, RPI18372, RPI18373, RPI18374, RPI18303, RPI18405, RPI18406, RPI18407, RPI18408, RPI18409, RPI18410, RPI18411, RPI18418, RPI18419, and RPI18422) have been identified which cause a
30 reduction in the levels of HBsAg and/or HBeAg as compared to the corresponding SAC ribozyme. In addition, loop variant anti-HBV ribozymes targeting site 273 were tested using this system, the results of this study are summarized in **Figure 10**. As indicated in the figure, the ribozymes tested demonstrate significant reduction in HepG2 HBsAg levels as compared
35 to a scrambled attenuated core ribozyme control, with RPI 22650 and RPI 22649 showing the greatest decrease in HBsAg levels.

Example 6: Analysis of HBsAg and SEAP Levels Following Ribozyme Treatment

Immulon 4 (Dynax) microtiter wells were coated overnight at 4° C with anti-HBsAg Mab (Biostride B88-95-31ad,ay) at 1 µg/ml in Carbonate Buffer (Na₂CO₃ 15 mM, NaHCO₃ 35 mM, pH 9.5). The wells were then washed 4x with PBST (PBS, 0.05% Tween® 20) and
 5 blocked for 1 hr at 37° C with PBST, 1% BSA. Following washing as above, the wells were dried at 37° C for 30 min. Biotinylated goat ant-HBsAg (Accurate YVS1807) was diluted 1:1000 in PBST and incubated in the wells for 1 hr. at 37° C. The wells were washed 4x with PBST. Streptavidin/Alkaline Phosphatase Conjugate (Pierce 21324) was diluted to 250 ng/ml in PBST, and incubated in the wells for 1 hr. at 37° C. After washing as above, p-
 10 nitrophenyl phosphate substrate (Pierce 37620) was added to the wells, which were then incubated for 1 hr. at 37° C. The optical density at 405 nm was then determined. SEAP levels were assayed using the Great EscAPe® Detection Kit (Clontech K2041-1), as per the manufacturers instructions.

Example 7: X-gene Reporter Assay

15 The effect of ribozyme treatment on the level of transactivation of a SV40 promoter driven firefly luciferase gene by the HBV X-protein was analyzed in transfected Hep G2 cells. As a control for variability in transfection efficiency, a Renilla luciferase reporter driven by the TK promoter, which is not transactivated by the X protein, was used. Hep G2 cells were plated (3 x 10⁴ cells/well) in 96-well microtiter plates and incubated overnight. A
 20 lipid/DNA/ribozyme complex was formed containing (at final concentrations) cationic lipid (2.4 µg/ml), the X-gene vector pSBDR(2.5 µg/ml), the firefly reporter pSV40HCVluc (0.5 µg/ml), the Renilla luciferase control vector pRL-TK (0.5 µg/ml), and ribozyme (100 µM). Following a 15 min. incubation at 37° C, the complexes were added to the plated Hep G2 cells. Levels of firefly and Renilla luciferase were analyzed 48 hr. post transfection, using
 25 Promega's Dual-Luciferase Assay System.

The HBV X protein is a transactivator of a number of viral and cellular genes. Ribozymes which target the X region were tested for their ability to cause a reduction in X protein transactivation of a firefly luciferase gene driven by the SV40 promoter in transfected Hep G2 cells. As a control for transfection variability, a vector containing the Renilla
 30 luciferase gene driven by the TK promotor, which is not activated by the X protein, was included in the co-transfections. The efficacy of the HBV ribozymes was determined by comparing the ratio of firefly luciferase: Renilla luciferase to that of a scrambled attenuated control (SAC) ribozyme. Eleven ribozymes (RPI18365, RPI18367, RPI18368, RPI18371, RPI18372, RPI18373, RPI18405, RPI18406, RPI18411, RPI18418, RPI18423) were
 35 identified which cause a reduction in the level of transactivation of a reporter gene by the X protein, as compared to the corresponding SAC ribozyme.

Example 8: HBV transgenic mouse study A

A transgenic mouse strain (founder strain 1.3.32 with a C57B1/6 background) that expresses HBV RNA and forms HBV viremia (Morrey *et al.*, 1999, *Antiviral Res.*, 42, 97-108; Guidotti *et al.*, 1995, *J. Virology*, 69, 10, 6158-6169) was utilized to study the *in vivo* activity of ribozymes (RPI.18341, RPI.18371, RPI.18372, and RPI.18418) of the instant invention. This model is predictive in screening for anti-HBV agents. Ribozyme or the equivalent volume of saline was administered via a continuous s.c. infusion using Alzet® mini-osmotic pumps for 14 days. Alzet® pumps were filled with test material(s) in a sterile fashion according to the manufacturer's instructions. Prior to *in vivo* implantation, pumps were incubated at 37°C overnight (\geq 18 hours) to prime the flow modulators. On the day of surgery, animals were lightly anesthetized with a ketamine/xylazine cocktail (94 mg/kg and 6 mg/kg, respectively; 0.3 ml, IP). Baseline blood samples (200 μ l) were obtained from each animal *via* a retro-orbital bleed. For animals in groups 1-5 (**Table XII**), a 2 cm area near the base of the tail was shaved and cleansed with betadine surgical scrub and sequentially with 70% alcohol. A 1 cm incision in the skin was made with a #15 scalpel blade or a blunt pair of scissors near the base of the tail. Forceps were used to open a pocket rostrally (*ie.*, towards the head) by spreading apart the subcutaneous connective tissue. The pump was inserted with the delivery portal pointing away from the incision. Wounds were closed with sterile 9-mm stainless steel clips or with sterile 4-0 suture. Animals were then allowed to recover from anesthesia on a warm heating pad before being returned to their cage. Wounds were checked daily. Clips or sutures were replaced as needed. Incisions typically healed completely within 7 days post-op. Animals were then deeply anesthetized with the ketamine/xylazine cocktail (150 mg/kg and 10 mg/kg, respectively; 0.5 ml, IP) on day 14 post pump implantation. A midline thoracotomy/ laparotomy was performed to expose the abdominal cavity and the thoracic cavity. The left ventricle was cannulated at the base and animals exsanguinated using a 23G needle and 1 ml syringe. Serum was separated, frozen and analyzed for HBV DNA and antigen levels. Experimental groups were compared to the saline control group in respect to percent change from day 0 to day 14. HBV DNA was assayed by quantitative PCR.

Results

Table XII is a summary of the group designation and dosage levels used in this HBV transgenic mouse study. Baseline blood samples were obtained *via* a retroorbital bleed and animals (N=10/group) received anti-HBV ribozymes (100 mg/kg/day) as a continuous SC infusion. After 14 days, animals treated with a ribozyme targeting site 273 (RPI.18341) of the HBV RNA showed a significant reduction in serum HBV DNA concentration, compared to the saline treated animals as measured by a quantitative PCR assay. More specifically, the

saline treated animals had a 69% increase in serum HBV DNA concentrations over this 2-week period while treatment with the 273 ribozyme (RPI.18341) resulted in a 60% decrease in serum HBV DNA concentrations. Ribozymes directed against sites 1833 (RPI.18371), 1873 (RPI.18418), and 1874 (RPI.18372) decreased serum HBV DNA concentrations by 49%, 15% and 16%, respectively.

Example 9: HBV transgenic mouse study B

A transgenic mouse strain (founder strain 1.3.32 with a C57B1/6 background) that expresses HBV RNA and forms HBV viremia (Morrey *et al.*, 1999, *Antiviral Res.*, 42, 97-108; Guidotti *et al.*, 1995, *J. Virology*, 69, 10, 6158-6169) was utilized to study the *in vivo* activity of ribozymes (RPI.18341 and RPI.18371) of the instant invention. This model is predictive in screening for anti-HBV agents. Ribozyme or the equivalent volume of saline was administered via a continuous s.c. infusion using Alzet® mini-osmotic pumps for 14 days. Alzet® pumps were filled with test material(s) in a sterile fashion according to the manufacturer's instructions. Prior to *in vivo* implantation, pumps were incubated at 37°C overnight (\geq 18 hours) to prime the flow modulators. On the day of surgery, animals were lightly anesthetized with a ketamine/xylazine cocktail (94 mg/kg and 6 mg/kg, respectively; 0.3 ml, IP). Baseline blood samples (200 μ l) were obtained from each animal *via* a retro-orbital bleed. For animals in groups 1-10 (**Table XIII**), a 2 cm area near the base of the tail was shaved and cleansed with betadine surgical scrub and sequentially with 70% alcohol. A 1 cm incision in the skin was made with a #15 scalpel blade or a blunt pair of scissors near the base of the tail. Forceps were used to open a pocket rostrally (*ie.*, towards the head) by spreading apart the subcutaneous connective tissue. The pump was inserted with the delivery portal pointing away from the incision. Wounds were closed with sterile 9-mm stainless steel clips or with sterile 4-0 suture. Animals were then allowed to recover from anesthesia on a warm heating pad before being returned to their cage. Wounds were checked daily. Clips or sutures were replaced as needed. Incisions typically healed completely within 7 days post-op. Animals were then deeply anesthetized with the ketamine/xylazine cocktail (150 mg/kg and 10 mg/kg, respectively; 0.5 ml, IP) on day 14 post pump implantation. A midline thoracotomy/ laparotomy was performed to expose the abdominal cavity and the thoracic cavity. The left ventricle was cannulated at the base and animals exsanguinated using a 23G needle and 1 ml syringe. Serum was separated, frozen and analyzed for HBV DNA and antigen levels. Experimental groups were compared to the saline control group in respect to percent change from day 0 to day 14. HBV DNA was assayed by quantitative PCR. Additionally, mice treated with 3TC® by oral gavage at a dose of 300 mg/kg/day for 14 days (group 11, **Table XIII**) were used as a positive control.

Results

Table XIII is a summary of the group designation and dosage levels used in this HBV transgenic mouse study. Baseline blood samples were obtained *via* a retroorbital bleed and animals (N=15/group) received anti-HBV ribozymes (100 mg/kg/day, 30 mg/kg/day, 10 mg/kg/day) as a continuous SC infusion. The results of this study are summarized in **Figures 6, 7, and 8**. As **Figures 6, 7, and 8** demonstrate, Ribozymes directed against sites 273 (RPI.18341) and 1833 (RPI.18371) demonstrate reduction in the serum HBV DNA levels following 14 days of ribozyme treatment in HBV transgenic mice, as compared to scrambled attenuated core (SAC) ribozyme and saline controls. Furthermore, these ribozymes provide similar, and in some cases, greater reduction of serum HBV DNA levels, as compared to the 3TC® positive control, at lower doses than the 3TC® positive control.

Example 10: HBV DNA reduction in HepG2.2.15 cells

Ribozyme treatment of HepG2.2.15 cells was performed in a 96-well plate format, with 12 wells for each different ribozyme tested (RPI.18341, RPI.18371, RPI.18372, RPI.18418, RPI.20599SAC). HBV DNA levels in the media collected between 120 and 144 hours following transfection was determined using the Roche Amplicor HBV Assay. Treatment with RPI.18341 targeting site 273 resulted in a significant ($P<0.05$) decrease in HBV DNA levels of 62% compared to the SAC (RPI.20599). Treatment with RPI.18371 (site 1833) or RPI.18372 (site 1874) resulted in reductions in HBV DNA levels of 55% and 58% respectively, as compared to treatment with the SAC RPI.20599 (see **Figure 9**).

Example 11: RPI 18341 combination treatment with Lamivudine/Infergen®

The therapeutic use of nucleic acid molecules of the invention either alone or in combination with current therapies, for example lamivudine or type 1 IFN, can lead to improved HBV treatment modalities. To assess the potential of combination therapy, HepG2 cells transfected with a replication competent HBV cDNA, were treated with RPI 18341(HepBzyme™), Infergen® (Amgen, Thousand Oaks Ca), and/or Lamivudine (Epivir®: GlaxoSmithKline, Research Triangle Park NC) either alone or in combination. Results indicated that combination treatment with either RPI 18341 plus Infergen® or combination of RPI 18341 plus lamivudine results in additive down regulation of HBsAg expression ($P<0.001$). These studies can be applied to the treatment of lamivudine resistant cells to further assess the potential for combination therapy of RPI 18341 plus currently available therapies for the treatment of chronic Hepatitis B.

Hep G2 cells were plated (2×10^4 cells/well) in 96-well microtiter plates and incubated overnight. A cationic lipid/DNA/ribozyme complex was formed containing (at final

concentrations) lipid (11-15 $\mu\text{g/mL}$), re-ligated psHBV-1 (4.5 $\mu\text{g/mL}$) and ribozyme (100-200 nM) in growth media. Following a 15 min incubation at 37°C, 20 μL of the complex was added to the plated Hep G2 cells in 80 μL of growth media minus antibiotics. For combination treatment with interferon, interferon (Infergen®, Amgen, Thousand Oaks CA) was added at 24 hr post-transfection and then incubated for an additional 96 hr. In the case of co-treatment with Lamivudine (3TC®), the ribozyme-containing cell culture media was removed at 120 hr post-transfection, fresh media containing Lamivudine (Epivir®: GlaxoSmithKline, Research Triangle Park NC) was added, and then incubated for an additional 48 hours. Treatment with Lamivudine or interferon individually was done on Hep G2 cells transfected with the pSHBV-1 vector alone and then treated identically to the co-treated cells. All transfections were performed in triplicate. Analysis of HBsAg levels was performed using the Diasorin HBsAg ELISA kit.

Results

At either 500 or 1000 units of Infergen®, the addition of 200 nM of RPI.18341 results in a 75-77% increase in anti-HBV activity as judged by the level of HBsAg secreted from the treated Hep G2 cells. Conversely, the anti-HBV activity of RPI.18341(at 200 nM) is increased 31-39% when used in combination of 500 or 1000 units of Infergen® (**Figure 11**).

At 25 nM Lamivudine (3TC®), the addition of 100 nM of RPI.18341 results in a 48% increase in anti-HBV activity as judged by the level of HBsAg secreted from treated Hep G2 cells. Conversely, the anti-HBV activity of RPI.18341 (at 100 nM) is increased 31% when used in combination with 25 nM Lamivudine (**Figure 12**).

Example 13: Modulation of HBV reverse transcriptase

The HBV reverse transcriptase (pol) binds to the 5' stem-loop structure in the HBV pregenomic RNA and synthesizes a four-nucleotide primer from the template UUCA. The reverse transcriptase then translocates to the 3' end of the pregenomic RNA where the primer binds to the UUCA sequence within the DR1 element and begins first-strand synthesis of HBV DNA. A number of short oligos, ranging in size from 4 to 16-mers, were designed to act as competitive inhibitors of the HBV reverse transcriptase primer, either by blocking the primer binding sites on the HBV RNA or by acting as a decoy.

The oligonucleotides and controls were synthesized in all 2'-O-methyl and 2'-O-allyl versions (**Table XV**). The inverse sequence of all oligos were generated to serve as controls. Primary screening of the competitive inhibitors was completed in the HBsAg transfection/ELISA system, in which the oligo is co-transfected with a HBV cDNA vector into Hep G2 cells. Following 4 days of incubation, the levels of HBsAg secreted into the cell

culture media were determined by ELISA. Screening of the 2'-O-allyl versions revealed that two of the decoy oligos (RPI.24944 and RPI.24945), consisting of 3x or 4x repeats of the RT primer binding site UUCA, along with the matched inverse controls, displayed considerable activity by decreasing HBsAg levels (**Figure 15**). This dramatic decrease in HBsAg levels is not due to cellular toxicity, because a MTS assay showed no difference in proliferation between any of the treated cells. A follow up experiment with a 5x UUCA repeat, the inverse sequence control, and a matched scrambled control, showed that all three oligos decreased HBsAg levels without cellular toxicity. Screening of the 2'-O-methyl versions of the oligos showed no activity from the 3x and 4x UUCA repeat (**Figure 16**), also suggesting that the anti-HBV effect is perhaps related to the 2'-O-allyl chemistry rather than to sequence specificity.

Screening of the 2'-O-methyl oligos did show that the 2'-O-methyl 2x UUCA repeat, RPI.24986, displayed activity in decreasing HBsAg levels as compared to the inverse control, RPI.24950. A dose response experiment showed that at the lower concentrations of 100 and 200 nM, RPI.24986 showed greater activity in decreasing HbsAg levels as compared to the inverse control RPI.24950 (**Figure 17**).

Example 14: Modulation of HBV transcription via Oligonucleotides targeting the Enhancer I core region of HBV DNA

In an effort to block HBV replication, oligonucleotides were designed to bind to two liver-specific factor binding sites in the Enhancer I core region of HBV genomic DNA. Hepatocyte Nuclear Factor 3 (HNF3) and Hepatocyte Nuclear Factor 4 (HNF4) bind to sites in the core region, with the HNF3 site being 5' to the HNF4 site. The HNF3 and HNF4 sites overlap or are adjacent to binding sites for a number of more ubiquitous factors, and are termed nuclear receptor response elements (NRRE). These elements are critical in regulating HBV transcription and replication in infected hepatocytes, with mutations in the HNF3 and HNF4 binding sites having been demonstrated to greatly reduce the levels of HBV replication (Bock *et al.*, 2000, *J. Virology*, 74, 2193)

Oligonucleotides (**Table XV**) were designed to bind to either the positive or negative strands of the HNF3 or HNF4 binding sites. Scrambled controls were made to match each oligo. Each oligo was synthesized in all 2'-O-methyl/all phosphorothioate, or all 2'-O-allyl/all phosphorothioate chemistries. The initial screening of the oligos was done in the HBsAg transfection/ELISA system in Hep G2 cells. RPI.25654, which targets the negative strand of the HNF4 binding site, shows greater activity in reducing HBsAg levels as compared to RPI.25655, which targets the HNF4 site positive strand, and the scrambled control RPI.25656. This result was observed at both 200 and 400 nM (**Figures 18 and 19**).

In a follow-up study, RPI.25654 reduced HBsAg levels in a dose-dependent manner, from 50-200 nM (**Figure 20**).

Example 15: Transfection of HepG2 Cells with psHBV-1 and Nucleic acid

The human hepatocellular carcinoma cell line Hep G2 was grown in Dulbecco's modified Eagle media supplemented with 10% fetal calf serum, 2 mM glutamine, 0.1 mM nonessential amino acids, 1 mM sodium pyruvate, 25 mM Hepes, 100 units penicillin, and 100 µg/ml streptomycin. To generate a replication competent cDNA, prior to transfection the HBV genomic sequences are excised from the bacterial plasmid sequence contained in the psHBV-1 vector. This was done with an EcoRI and Hind III restriction digest. Following completion of the digest, a ligation was performed under dilute conditions (20 µg/ml) to favor intermolecular ligation. The total ligation mixture was then concentrated using Qiagen spin columns. One skilled in the art would realize that other methods can be used to generate a replication competent cDNA.

Secreted alkaline phosphatase (SEAP) was used to normalize the HBsAg levels to control for transfection variability. The pSEAP2-TK control vector was constructed by ligating a Bgl II-Hind III fragment of the pRL-TK vector (Promega), containing the herpes simplex virus thymidine kinase promoter region, into Bgl II/Hind III digested pSEAP2-Basic (Clontech). Hep G2 cells were plated (3×10^4 cells/well) in 96-well microtiter plates and incubated overnight. A lipid/DNA/nucleic acid complex was formed containing (at final concentrations) cationic lipid (15 µg/ml), prepared psHBV-1 (4.5 µg/ml), pSEAP2-TK (0.5 µg/ml), and nucleic acid (100 µM). Following a 15 min. incubation at 37° C, the complexes were added to the plated Hep G2 cells. Media was removed from the cells 96 hr. post-transfection for HBsAg and SEAP analysis.

Transfection of the human hepatocellular carcinoma cell line, Hep G2, with replication competent HBV DNA results in the expression of HBV proteins and the production of virions.

Example 16: Analysis of HBsAg and SEAP Levels Following Nucleic Acid Treatment

Immulon 4 (Dynax) microtiter wells were coated overnight at 4° C with anti-HBsAg Mab (Biostride B88-95-31ad,ay) at 1 µg/ml in Carbonate Buffer (Na₂CO₃ 15 mM, NaHCO₃ 35 mM, pH 9.5). The wells were then washed 4x with PBST (PBS, 0.05% Tween® 20) and blocked for 1 hr at 37° C with PBST, 1% BSA. Following washing as above, the wells were dried at 37° C for 30 min. Biotinylated goat anti-HBsAg (Accurate YVS1807) was diluted 1:1000 in PBST and incubated in the wells for 1 hr. at 37° C. The wells were washed 4x with PBST. Streptavidin/Alkaline Phosphatase Conjugate (Pierce 21324) was diluted to 250

ng/ml in PBST, and incubated in the wells for 1 hr. at 37° C. After washing as above, p-nitrophenyl phosphate substrate (Pierce 37620) was added to the wells, which were then incubated for 1 hr. at 37° C. The optical density at 405 nm was then determined. SEAP levels were assayed using the Great EscAPe® Detection Kit (Clontech K2041-1), as per the manufacturers instructions.

Example 17: Analysis of HBV DNA expression a HepG2.2.15 murine model

The development of new antiviral agents for the treatment of chronic Hepatitis B has been aided by the use of animal models that are permissive to replication of related Hepadnaviridae such as Woodchuck Hepatitis Virus (WHV) and Duck Hepatitis Virus (DHV). In addition, the use of transgenic mice has also been employed. The human hepatoblastoma cell line, HepG2.2.15, implanted as a subcutaneous (SC) tumor, can be used to produce Hepatitis B viremia in mice. This model is useful for evaluating new HBV therapies. Mice bearing HepG2.2.15 SC tumors show HBV viremia. HBV DNA can be detected in serum beginning on Day 35. Maximum serum viral levels reach 1.9×10^5 copies/mL by day 49. A study also determined that the minimum tumor volume associated with viremia was 300 mm³. Therefore, the HepG2.2.15 cell line grown as a SC tumor produces a useful model of HBV viremia in mice. This new model can be suitable for evaluating new therapeutic regimens for chronic Hepatitis B.

HepG2.2.15 tumor cells contain a slightly truncated version of viral HBV DNA and sheds HBV particles. The purpose of this study was to identify what time period viral particles are shed from the tumor. Serum was analyzed for presence of HBV DNA over a time course after HepG2.2.15 tumor inoculation in Athymic Ncr nu/nu mice. HepG2.2.15 cells were carried and expanded in DMEM/10% FBS/2.4% HEPES/1% NEAA/1% Glutamine/1% Sodium Pyruvate media. Cells were resuspended in Delbecco's PBS with calcium/magnesium for injection. One hundred microliters of the tumor cell suspension (at a concentration of 1×10^8 cells/mL) were injected subcutaneously in the flank of NCR nu/nu female mice with a 23g1 needle and 1 cc syringe, thereby giving each mouse 1×10^7 cells. Tumors were allowed to grow for a period of up to 49 days post tumor cell inoculation. Serum was sampled for analysis on days 1, 7, 14, 35, 42 and 49 post tumor inoculation. Length and width measurements from each tumor were obtained three times per week using a Jamison microcaliper. Tumor volumes were calculated from tumor length/width measurements (tumor volume = $0.5[a(b)^2]$ where a = longest axis of the tumor and b = shortest axis of the tumor). Serum was analyzed for the presence of HBV DNA by the Roche Amplicor HBV monitor TM DNA assay.

Experiment 1

HepG2.2.15 cells were carried and expanded in DMEM/10% FBS/2.4%HEPES/1%NEAA/1% Glutamine/1% Sodium Pyruvate media. Cells were resuspended in Delbecco's PBS with calcium/magnesium for injection. One hundred microliters of the tumor cell suspension (at a concentration of 1×10^8 cells/mL) were injected subcutaneously in the flank of NCR nu/nu female mice with a 23g1 needle and 1 cc syringe, thereby giving each mouse 1×10^7 cells. Tumors were allowed to grow for a period of up to 49 days post tumor cell inoculation. Serum was sampled for analysis on days 1, 7, 14, 35, 42 and 49 post tumor inoculation. Length and width measurements from each tumor were obtained three times per week using a Jamison microcaliper. Tumor volumes were calculated from tumor length/width measurements (tumor volume = $0.5[a(b)^2]$ where a = longest axis of the tumor and b = shortest axis of the tumor). Serum was analyzed for the presence of HBV DNA by the Roche Amplicor HBV monitor TM DNA assay.

Results

When athymic nu/nu female mice are subcutaneously injected with HepG2.2.15 cells and form tumors, HBV DNA is detected in serum (peak serum level was 1.9×10^5 copies/mL). There is a positive correlation ($r_s = 0.7$, $p < 0.01$) between tumor weight (milligrams) and HB viral copies/mL serum. **Figure 21** shows a plot of HepG2.2.15 tumors in nu/nu female mice as tumor volume vs time. **Table XVI** shows the concentration of HBV DNA in relation to tumor size in the HepG2.2.15 implanted nu/nu female mice used in the study.

Experiment 2

HepG2.2.15 cells were carried and expanded in DMEM/10% FBS/2.4%HEPES/1%NEAA/1% Glutamine/1% Sodium Pyruvate media containing 400 µg/ml G418 antibiotic. G418-resistant cells were resuspended in Dulbecco's PBS with calcium/magnesium for injection. One hundred microliters of the tumor cell suspension (at a concentration of 1×10^8 cells/mL) were injected subcutaneously in the flank of NCR nu/nu female mice with a 23g1 needle and 1 cc syringe, thereby giving each mouse 1×10^7 cells. Tumors were allowed to grow for a period of up to 49 days post tumor cell inoculation. Serum was sampled for analysis on day 37 post tumor inoculation. Length and width measurements from each tumor were obtained three times per week using a Jamison microcaliper. Tumor volumes were calculated from tumor length/width measurements (tumor volume = $0.5[a(b)^2]$ where a = longest axis of the tumor and b = shortest axis of the tumor). Serum was analyzed for the presence of HBV DNA by the Roche Amplicor HBV monitor TM DNA assay.

Results

When athymic nu/nu female mice are subcutaneously injected with G418 antibiotic resistant HepG2.2.15 cells and form tumors, HBV DNA is detected in serum (peak serum level was 4.0×10^5 copies/mL). There is a positive correlation ($r_s = 0.7$, $p < 0.01$) between tumor weight (milligrams) and HB viral copies/mL serum. **Figure 22** shows a plot of HepG2.2.15 tumors in nu/nu female mice as tumor volume vs time. **Table XVII** shows the concentration of HBV DNA in relation to tumor size in the G418 antibiotic resistant HepG2.2.15 implanted nu/nu female mice used in the study.

Example 18: Identification of Potential Enzymatic nucleic acid molecules Cleavage Sites in HCV RNA

The sequence of HCV RNA was screened for accessible sites using a computer folding algorithm. Regions of the mRNA that did not form secondary folding structures and contained potential enzymatic nucleic acid cleavage sites were identified. The sequences of these cleavage sites are shown in **Tables XVIII, XIX, XX and XXIII**.

Example 19: Selection of Enzymatic nucleic acid molecules Cleavage Sites in HCV RNA

Enzymatic nucleic acid target sites were chosen by analyzing sequences of Human HCV (Genbank accession Nos: D11168, D50483.1, L38318 and S82227) and prioritizing the sites on the basis of folding. Enzymatic nucleic acid molecules are designed that could bind each target and are individually analyzed by computer folding (Christoffersen *et al.*, 1994 *J. Mol. Struc. Theochem*, 311, 273; Jaeger *et al.*, 1989, *Proc. Natl. Acad. Sci. USA*, 86, 7706) to assess whether the enzymatic nucleic acid molecules sequences fold into the appropriate secondary structure. Those enzymatic nucleic acid molecules with unfavorable intramolecular interactions between the binding arms and the catalytic core can be eliminated from consideration. As noted below, varying binding arm lengths can be chosen to optimize activity. Generally, at least 4 bases on each arm are able to bind to, or otherwise interact with, the target RNA.

Example 20: Chemical Synthesis and Purification of Enzymatic nucleic acids

Enzymatic nucleic acid molecules can be designed to anneal to various sites in the RNA message. The binding arms of the enzymatic nucleic acid molecules are complementary to the target site sequences described above. The enzymatic nucleic acid molecules can be chemically synthesized using, for example, RNA syntheses such as those described above and those described in Usman *et al.*, (1987 *J. Am. Chem. Soc.*, 109, 7845), Scaringe *et al.*, (1990 *Nucleic Acids Res.*, 18, 5433) and Wincott *et al.*, *supra*. Such methods make use of common nucleic acid protecting and coupling groups, such as dimethoxytrityl at the 5'-end, and phosphoramidites at the 3'-end. The average stepwise coupling yields are

typically >98%. Enzymatic nucleic acid molecules can be modified to enhance stability by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-fluoro, 2'-O-methyl, 2'-H (for a review see Usman and Cedergren, 1992 TIBS 17, 34).

Enzymatic nucleic acid molecules can also be synthesized from DNA templates using bacteriophage T7 RNA polymerase (Milligan and Uhlenbeck, 1989, Methods Enzymol. 180, 51). Enzymatic nucleic acid molecules can be purified by gel electrophoresis using known methods, or can be purified by high pressure liquid chromatography (HPLC; See Wincott et al., supra; the totality of which is hereby incorporated herein by reference), and are resuspended in water. The sequences of chemically synthesized enzymatic nucleic acid constructs are shown below in **Tables XX, XXI and XXIII**. The antisense nucleic acid molecules shown in **Table XXII** were chemically synthesized.

Inactive enzymatic nucleic acid molecules, for example inactive hammerhead enzymatic nucleic acids, can be synthesized by substituting the order of G5A6 and substituting a U for A14 (numbering from Hertel et al., 1992 Nucleic Acids Res., 20, 3252).

15 Example 21: Enzymatic Nucleic Acid Cleavage of HCV RNA Target *in vitro*

Enzymatic nucleic acid molecules targeted to the HCV are designed and synthesized as described above. These enzymatic nucleic acid molecules can be tested for cleavage activity *in vitro*, for example using the following procedure. The target sequences and the nucleotide location within the HCV are given in **Tables XVIII, XIX, XX and XXIII**.

20 *Cleavage Reactions:* Full-length or partially full-length, internally-labeled target RNA for enzymatic nucleic acid molecule cleavage assay is prepared by *in vitro* transcription in the presence of [α - 32 P] CTP, passed over a G 50 Sephadex column by spin chromatography and used as substrate RNA without further purification. Alternately, substrates are 5'- 32 P-end labeled using T4 polynucleotide kinase enzyme. Assays are performed by pre-warming a 2X
25 concentration of purified enzymatic nucleic acid molecule in enzymatic nucleic acid molecule cleavage buffer (50 mM Tris-HCl, pH 7.5 at 37°C, 10 mM MgCl₂) and the cleavage reaction was initiated by adding the 2X enzymatic nucleic acid molecule mix to an equal volume of substrate RNA (maximum of 1-5 nM) that was also pre-warmed in cleavage buffer. As an initial screen, assays are carried out for 1 hour at 37°C using a final
30 concentration of either 40 nM or 1 mM enzymatic nucleic acid molecule, *i.e.*, enzymatic nucleic acid molecule excess. The reaction is quenched by the addition of an equal volume of 95% formamide, 20 mM EDTA, 0.05% bromophenol blue and 0.05% xylene cyanol after which the sample is heated to 95°C for 2 minutes, quick chilled and loaded onto a denaturing polyacrylamide gel. Substrate RNA and the specific RNA cleavage products generated by
35 enzymatic nucleic acid molecule cleavage are visualized on an autoradiograph of the gel. The

percentage of cleavage is determined by Phosphor Imager[®] quantitation of bands representing the intact substrate and the cleavage products.

Alternatively, enzymatic nucleic acid molecules and substrates were synthesized in 96-well format using 0.2μmol scale. Substrates were 5'-³²P labeled and gel purified using 7.5% polyacrylamide gels, and eluting into water. Assays were done by combining trace substrate with 500nM enzymatic nucleic acid or greater, and initiated by adding final concentrations of 40mM Mg⁺², and 50mM Tris-Cl pH 8.0. For each enzymatic nucleic acid/substrate combination a control reaction was done to ensure cleavage was not the result of non-specific substrate degradation. A single three hour time point was taken and run on a 15% polyacrylamide gel to assess cleavage activity. Gels were dried and scanned using a Molecular Dynamics Phosphorimager and quantified using Molecular Dynamics ImageQuant software. Percent cleaved was determined by dividing values for cleaved substrate bands by full-length (uncleaved) values plus cleaved values and multiplying by 100 (%cleaved=[C/(U+C)]*100). In vitro cleavage data of enzymatic nucleic acid molecules targeting plus and minus strand HCV RNA is shown in **Table XXIII**.

Example 22: Inhibition of Luciferase Activity Using HCV Targeting Enzymatic nucleic acids in OST7 Cells

The capability of enzymatic nucleic acids to inhibit HCV RNA intracellularly was tested using a dual reporter system that utilizes both firefly and Renilla luciferase (**Figure 23**). The enzymatic nucleic acids targeted to the 5' HCV UTR region, which when cleaved, would prevent the translation of the transcript into luciferase.

Synthesis of Stabilized Enzymatic nucleic acids

Enzymatic nucleic acids were designed to target 15 sites within the 5'UTR of the HCV RNA (**Figure 24**) and synthesized as previously described, except that all enzymatic nucleic acids contain two 2'-amino uridines. Enzymatic nucleic acid and paired control sequences for targeted sites used in various examples herein are shown in **Table XXI**.

Reporter plasmids

The T7/HCV/firefly luciferase plasmid (HCVT7C₁₋₃₄₁, genotype 1a) was graciously provided by Aleem Siddiqui (University of Colorado Health Sciences Center, Denver, CO). The T7/HCV/firefly luciferase plasmid contains a T7 bacteriophage promoter upstream of the HCV 5'UTR (nucleotides 1-341)/firefly luciferase fusion DNA. The Renilla luciferase control plasmid (pRLSV40) was purchased from PROMEGA.

Luciferase assay

Dual luciferase assays were carried out according to the manufacturer's instructions (PROMEGA) at 4 hours after co-transfection of reporter plasmids and enzymatic nucleic acids. All data is shown as the average ratio of HCV/firefly luciferase luminescence over Renilla luciferase luminescence as determined by triplicate samples \pm SD.

5 Cell culture and transfections

OST7 cells were maintained in Dulbecco's modified Eagle's medium (GIBCO BRL) supplemented with 10% fetal calf serum, L-glutamine (2 mM) and penicillin/streptomycin. For transfections, OST7 cells were seeded in black-walled 96-well plates (Packard) at a density of 12,500 cells/well and incubated at 37°C under 5% CO₂ for 24 hours. Co-transfection of target reporter HCV7C (0.8 µg/mL), control reporter pRLSV40, (1.2 µg/mL) and enzymatic nucleic acid, (50 - 200 nM) was achieved by the following method: a 5X mixture of HCV7C (4 µg/mL), pRLSV40 (6 µg/mL) enzymatic nucleic acid (250 – 1000 nM) and cationic lipid (28.5 µg/mL) was made in 150 µL of OPTI-MEM (GIBCO BRL) minus serum. Reporter/enzymatic nucleic acid/lipid complexes were allowed to form for 20 min at 37°C under 5% CO₂. Medium was aspirated from OST7 cells and replaced with 120 µL of OPTI-MEM (GIBCO BRL) minus serum, immediately followed by the addition of 30 µL of 5X reporter/enzymatic nucleic acid/lipid complexes. Cells were incubated with complexes for 4 hours at 37°C under 5% CO₂.

IC50 determinations for dose response curves

Apparent IC₅₀ values were calculated by linear interpolation. The apparent IC₅₀ is 1/2 the maximal response between the two consecutive points in which approximately 50% inhibition of HCV/luciferase expression is observed on the dose curve.

Quantitation of RNA Samples

Total RNA from transfected cells was purified using the Qiagen RNeasy 96 procedure including a DNase I treatment according to the manufacturer's instructions. Real time RT-PCR (Taqman assay) was performed on purified RNA samples using separate primer/probe sets specific for either firefly or Renilla luciferase RNA. Firefly luciferase primers and probe were upper (5'-CGGTCGGTAAAGTTGTTCCATT-3') (SEQ ID NO. 16202), lower (5'-CCTCTGACACATAATTCGCCTCT-3') (SEQ ID NO. 16203), and probe (5'-FAM-TGAAGCGAAGGTTGTGGATCTGGATACC-TAMRA-3') (SEQ ID NO 16204), and Renilla luciferase primers and probe were upper (5'-GTTTATTGAATCGGACCCAGGAT-3') (SEQ ID NO. 16205), lower (5'-AGGTGCATCTTCTTGCGAAAA-3') (SEQ ID NO. 16206), and probe (5'-FAM-CTTTTCCAATGCTATTGTTGAAGGTGCCAA-3') (SEQ ID NO. 16207) -TAMRA, both sets of primers and probes were purchased from Integrated DNA

Technologies. RNA levels were determined from a standard curve of amplified RNA purified from a large-scale transfection. RT minus controls established that RNA signals were generated from RNA and not residual plasmid DNA. RT-PCR conditions were: 30 min at 48°C, 10 min at 95°C, followed by 40 cycles of 15 sec at 95°C and 1 min at 60°C. Reactions were performed on an ABI Prism 7700 sequence detector. Levels of firefly luciferase RNA were normalized to the level of Renilla luciferase RNA present in the same sample. Results are shown as the average of triplicate treatments \pm SD.

Example 23: Inhibition of HCV 5'UTR-luciferase expression by synthetic stabilized enzymatic nucleic acids

The primary sequence of the HCV 5'UTR and characteristic secondary structure (**Figure 24**) is highly conserved across all HCV genotypes, thus making it a very attractive target for enzymatic nucleic acid-mediated cleavage. Enzymatic hammerhead nucleic acids, as a generally shown in **Figure 25** and **Table XXI** (RPI 12249-12254, 12257-12265) were designed and synthesized to target 15 of the most highly conserved sites in the 5'UTR of HCV RNA. These synthetic enzymatic nucleic acids were stabilized against nuclease degradation by the addition of modifications such as 2'-*O*-methyl nucleotides, 2'-amino-uridines at U4 and U7 core positions, phosphorothioate linkages, and a 3'-inverted abasic cap.

In order to mimic cytoplasmic transcription of the HCV genome, OST7 cells were transfected with a target reporter plasmid containing a T7 bacteriophage promoter upstream of a HCV 5'UTR/firefly luciferase fusion gene. Cytoplasmic expression of the target reporter is facilitated by high levels of T7 polymerase expressed in the cytoplasm of OST7 cells. Co-transfection of target reporter HCVT7C₁₋₃₄₁ (firefly luciferase), control reporter pRLSV40 (Renilla luciferase) and enzymatic nucleic acid was carried out in the presence of cationic lipid. To determine the background level of luciferase activity, applicant used a control enzymatic nucleic acid that targets an irrelevant, non-HCV sequence. Transfection of reporter plasmids in the presence of this irrelevant control enzymatic nucleic acid (ICR) resulted in a slight decrease of reporter expression when compared to transfection of reporter plasmids alone. Therefore, the ICR was used to control for non-specific effects on reporter expression during treatment with HCV specific enzymatic nucleic acids. Renilla luciferase expression from the pRLSV40 reporter was used to normalize for transfection efficiency and sample recovery.

Of the 15 amino-modified hammerhead enzymatic nucleic acids tested, 12 significantly inhibited HCV/luciferase expression ($> 45\%$, $P < 0.05$) as compared to the ICR (**Figure 26A**). These data suggest that most of the HCV 5'UTR sites targeted here are accessible to enzymatic nucleic acid binding and subsequent RNA cleavage. To investigate further the

enzymatic nucleic acid-dependent inhibition of HCV/luciferase activity, hammerhead enzymatic nucleic acids designed to cleave after sites 79, 81, 142, 192, 195, 282 or 330 of the HCV 5'UTR were selected for continued study because their anti-HCV activity was the most efficacious over several experiments. A corresponding attenuated core (AC) control was synthesized for each of the 7 active enzymatic nucleic acids (**Table XX**). Each paired AC control contains similar nucleotide composition to that of its corresponding active enzymatic nucleic acid however, due to scrambled binding arms and changes to the catalytic core, lacks the ability to bind or catalyze the cleavage of HCV RNA. Treatment of OST7 cells with enzymatic nucleic acids designed to cleave after sites 79, 81, 142, 195 or 330 resulted in significant inhibition of HCV/luciferase expression (65%, 50%, 50%, 80% and 80%, respectively) when compared to HCV/luciferase expression in cells treated with corresponding ACs, $P < 0.05$ (**Figure 26B**). It should be noted that treatment with either the ICR or ACs for sites 79, 81, 142 or 192 caused a greater reduction of HCV/luciferase expression than treatment with ACs for sites 195, 282 or 330. The observed differences in HCV/luciferase expression after treatment with ACs most likely represents the range of activity due to non-specific effects of oligonucleotide treatment and/or differences in base composition. Regardless of differences in HCV/luciferase expression levels observed as a result of treatment with ACs, active enzymatic nucleic acids designed to cleave after sites 79, 81, 142, 195, or 330 demonstrated similar and potent anti-HCV activity (**Figure 26B**).

Example 24: Synthetic stabilized enzymatic nucleic acids inhibit HCV/luciferase expression in a concentration-dependent manner

In order to characterize enzymatic nucleic acid efficacy in greater detail, these same 5 lead hammerhead enzymatic nucleic acids were tested for their ability to inhibit HCV/luciferase expression over a range of enzymatic nucleic acid concentrations (0 nM - 100 nM). For constant transfection conditions, the total concentration of nucleic acid was maintained at 100 nM for all samples by mixing the active enzymatic nucleic acid with its corresponding AC. Moreover, mixing of active enzymatic nucleic acid and AC maintains the lipid to nucleic acid charge ratio. A concentration-dependent inhibition of HCV/luciferase expression was observed after treatment with each of the 5 enzymatic nucleic acids (**Figures 27A-E**). By linear interpolation, the enzymatic nucleic acid concentration resulting in 50% inhibition (apparent IC_{50}) of HCV/luciferase expression ranged from 40 - 215 nM. The two most efficacious enzymatic nucleic acids were those designed to cleave after sites 195 or 330 with apparent IC_{50} values of 46 nM and 40 nM, respectively (**Figures 27D and E**).

Example 25: An enzymatic nucleic acid mechanism is required for the observed inhibition of HCV/luciferase expression

To confirm that an enzymatic nucleic acid mechanism of action was responsible for the observed inhibition of HCV/luciferase expression, paired binding-arm attenuated core (BAC) controls (RPI 15291 and 15294) were synthesized for direct comparison to enzymatic nucleic acids targeting sites 195 (RPI 12252) and 330 (RPI 12254). Paired BACs can specifically
 5 bind HCV RNA but are unable to promote RNA cleavage because of changes in the catalytic core and, thus, can be used to assess inhibition due to binding alone. Also included in this comparison were paired SAC controls (RPI 15292 and 15295) that contain scrambled binding arms and attenuated catalytic cores, and so lack the ability to bind the target RNA or to catalyze target RNA cleavage.

Enzymatic nucleic acid cleavage of target RNA should result in both a lower level of HCV/luciferase RNA and a subsequent decrease in HCV/luciferase expression. In order to analyze target RNA levels, a reverse transcriptase/polymerase chain reaction (RT-PCR) assay was employed to quantify HCV/luciferase RNA levels. Primers were designed to amplify the luciferase coding region of the HCV 5'UTR/luciferase RNA. This region was chosen because
 15 HCV-targeted enzymatic nucleic acids that might co-purify with cellular RNA would not interfere with RT-PCR amplification of the luciferase RNA region. Primers were also designed to amplify the Renilla luciferase RNA so that Renilla RNA levels could be used to control for transfection efficiency and sample recovery.

OST7 cells were treated with active enzymatic nucleic acids designed to cleave after
 20 sites 195 or 330, paired SACs, or paired BACs. Treatment with enzymatic nucleic acids targeting site 195 or 330 resulted in a significant reduction of HCV/luciferase RNA when compared to their paired SAC controls ($P < 0.01$). In this experiment the site 195 enzymatic nucleic acid was more efficacious than the site 330 enzymatic nucleic acid (**Figure 28A**). Treatment with paired BACs that target site 195 or 330 did not reduce HCV/luciferase RNA
 25 when compared to the corresponding SACs, thus confirming that the ability to bind alone does not result in a reduction of HCV/luciferase RNA.

To confirm that enzymatic nucleic acid-mediated cleavage of target RNA is necessary for inhibition of HCV/luciferase expression, HCV/luciferase activity was determined in the same experiment. As expected, significant inhibition of HCV/luciferase expression was
 30 observed after treatment with active enzymatic nucleic acids when compared to paired SACs (**Figure 28B**). Importantly, treatment with paired BACs did not inhibit HCV/luciferase expression, thus confirming that the ability to bind alone is also not sufficient to inhibit translation. As observed in the RNA assay, the site 195 enzymatic nucleic acid was more efficacious than the site 330 enzymatic nucleic acid in this experiment. However, a
 35 correlation between enzymatic nucleic acid-mediated HCV RNA reduction and inhibition of HCV/luciferase translation was observed for enzymatic nucleic acids to both sites. The

reduction in target RNA and the necessity for an active enzymatic nucleic acid catalytic core confirm that a enzymatic nucleic acid mechanism is required for the observed reduction in HCV/luciferase protein activity in cells treated with site 195 or site 330 enzymatic nucleic acids.

5 Example 26: Zinzyme Inhibition of chimeric HCV/Poliovirus replication

During HCV infection, viral RNA is present as a potential target for enzymatic nucleic acid cleavage at several processes: un-coating, translation, RNA replication and packaging. Target RNA can be more or less accessible to enzymatic nucleic acid cleavage at any one of these steps. Although the association between the HCV initial ribosome entry site (IRES) and the translation apparatus is mimicked in the HCV 5'UTR/luciferase reporter system, these other viral processes are not represented in the OST7 system. The resulting RNA/protein complexes associated with the target viral RNA are also absent. Moreover, these processes can be coupled in an HCV-infected cell which could further impact target RNA accessibility. Therefore, applicant tested whether enzymatic nucleic acids designed to cleave the HCV 5'UTR could effect a replicating viral system.

Recently, Lu and Wimmer characterized a HCV-poliovirus chimera in which the poliovirus IRES was replaced by the IRES from HCV (Lu & Wimmer, 1996, Proc. Natl. Acad. Sci. USA. 93, 1412-1417). Poliovirus (PV) is a positive strand RNA virus like HCV, but unlike HCV is non-enveloped and replicates efficiently in cell culture. The HCV-PV chimera expresses a stable, small plaque phenotype relative to wild type PV.

The following enzymatic nucleic acid molecules (zinzymes) were synthesized and tested for replicative inhibition of an HCV/Poliovirus chimera: RPI 18763, RPI 18812, RPI 18749, RPI 18765, RPI 18792, and RPI 18814 (**Table XX**). A scrambled attenuated core enzymatic nucleic acid, RPI 18743, was used as a control.

HeLa cells were infected with the HCV-PV chimera for 30 minutes and immediately treated with enzymatic nucleic acid. HeLa cells were seeded in U-bottom 96-well plates at a density of 9000-10,000 cells/well and incubated at 37°C under 5% CO₂ for 24 h. Transfection of nucleic acid (200 nM) was achieved by mixing of 10X nucleic acid (2000 nM) and 10X of a cationic lipid (80 µg/ml) in DMEM (Gibco BRL) with 5% fetal bovine serum (FBS). Nucleic acid/lipid complexes were allowed to incubate for 15 minutes at 37°C under 5% CO₂. Medium was aspirated from cells and replaced with 80 µl of DMEM (Gibco BRL) with 5% FBS serum, followed by the addition of 20 µls of 10X complexes. Cells were incubated with complexes for 24 hours at 37°C under 5% CO₂.

The yield of HCV-PV from treated cells was quantified by plaque assay. The plaque assays were performed by diluting virus samples in serum-free DMEM (Gibco BRL) and applying 100 µl to HeLa cell monolayers (~80% confluent) in 6-well plates for 30 minutes. Infected monolayers were overlaid with 3 ml 1.2% agar (Sigma) and incubated at 37°C under 5% CO₂. Two or three days later the overlay was removed, monolayers were stained with 1.2% crystal violet, and plaque forming units were counted. The results for the zinzyme inhibition of HCV-PV replication are shown in **Figure 33**.

Example 27: Antisense inhibition of chimeric HCV/Poliovirus replication

Antisense nucleic acid molecules (RPI 17501 and RPI 17498, **Table XXII**) were tested for replicative inhibition of an HCV/Poliovirus chimera compared to scrambled controls. An antisense nucleic acid molecule is a non-enzymatic nucleic acid molecule that binds to target RNA by means of RNA-RNA or RNA-DNA or RNA-PNA (protein nucleic acid; Egholm et al., 1993 Nature 365, 566) interactions and alters the activity of the target RNA (for a review, see Stein and Cheng, 1993 Science 261, 1004 and Woolf et al., US patent No. 5,849,902). Typically, antisense molecules are complementary to a target sequence along a single contiguous sequence of the antisense molecule. However, in certain embodiments, an antisense molecule can bind to substrate such that the substrate molecule forms a loop, and/or an antisense molecule can bind such that the antisense molecule forms a loop. Thus, the antisense molecule can be complementary to two (or even more) non-contiguous substrate sequences or two (or even more) non-contiguous sequence portions of an antisense molecule can be complementary to a target sequence or both. For a review of current antisense strategies, see Schmajuk et al., 1999, J. Biol. Chem., 274, 21783-21789, Delihias et al., 1997, Nature, 15, 751-753, Stein et al., 1997, Antisense N. A. Drug Dev., 7, 151, Crooke, 2000, Methods Enzymol., 313, 3-45; Crooke, 1998, Biotech. Genet. Eng. Rev., 15, 121-157, Crooke, 1997, Ad. Pharmacol., 40, 1-49. In addition, antisense DNA can be used to target RNA by means of DNA-RNA interactions, thereby activating RNase H, which digests the target RNA in the duplex. The antisense oligonucleotides can comprise one or more RNase H activating region, which is capable of activating RNase H cleavage of a target RNA. Antisense DNA can be synthesized chemically or expressed via the use of a single stranded DNA expression vector or equivalent thereof. Additionally, antisense molecules can be used in combination with the enzymatic nucleic acid molecules of the instant invention.

A RNase H activating region is a region (generally greater than or equal to 4-25 nucleotides in length, preferably from 5-11 nucleotides in length) of a nucleic acid molecule capable of binding to a target RNA to form a non-covalent complex that is recognized by cellular RNase H enzyme (see for example Arrow et al., US 5,849,902; Arrow et al., US 5,989,912). The RNase H enzyme binds to the nucleic acid molecule-target RNA complex

and cleaves the target RNA sequence. The RNase H activating region comprises, for example, phosphodiester, phosphorothioate (preferably at least four of the nucleotides are phosphorothioate substitutions; more specifically, 4-11 of the nucleotides are phosphorothioate substitutions); phosphorodithioate, 5'-thiophosphate, or methylphosphonate backbone chemistry or a combination thereof. In addition to one or more backbone chemistries described above, the RNase H activating region can also comprise a variety of sugar chemistries. For example, the RNase H activating region can comprise deoxyribose, arabino, fluoroarabino or a combination thereof, nucleotide sugar chemistry. Those skilled in the art will recognize that the foregoing are non-limiting examples and that any combination of phosphate, sugar and base chemistry of a nucleic acid that supports the activity of RNase H enzyme is within the scope of the definition of the RNase H activating region and the instant invention.

HeLa cells were infected with the HCV-PV chimera for 30 minutes and immediately treated with antisense nucleic acid. HeLa cells were seeded in U-bottom 96-well plates at a density of 9000-10,000 cells/well and incubated at 37°C under 5% CO₂ for 24 h. Transfection of nucleic acid (200 nM) was achieved by mixing of 10X nucleic acid (2000 nM) and 10X of a cationic lipid (80 µg/ml) in DMEM (Gibco BRL) with 5% fetal bovine serum (FBS). Nucleic acid/lipid complexes were allowed to incubate for 15 minutes at 37°C under 5% CO₂. Medium was aspirated from cells and replaced with 80 µl of DMEM (Gibco BRL) with 5% FBS serum, followed by the addition of 20 µls of 10X complexes. Cells were incubated with complexes for 24 hours at 37°C under 5% CO₂.

The yield of HCV-PV from treated cells was quantified by plaque assay. The plaque assays were performed by diluting virus samples in serum-free DMEM (Gibco BRL) and applying 100 µl to HeLa cell monolayers (~80% confluent) in 6-well plates for 30 minutes. Infected monolayers were overlaid with 3 ml 1.2% agar (Sigma) and incubated at 37°C under 5% CO₂. Two or three days later the overlay was removed, monolayers were stained with 1.2% crystal violet, and plaque forming units were counted. The results for the antisense inhibition of HCV-PV are shown in **Figure 34**.

Example 28: Nucleic acid Inhibition of Chimeric HCV/PV in combination with Interferon

One of the limiting factors in interferon (IFN) therapy for chronic HCV are the toxic side effects associated with IFN. Applicant has reasoned that lowering the dose of IFN needed can reduce these side effects. Applicant has previously shown that enzymatic nucleic acid molecules targeting HCV RNA have a potent antiviral effect against replication of an HCV-poliovirus (PV) chimera (Macejak *et al.*, 2000, *Hepatology*, 31, 769-776). In order to determine if the antiviral effect of type 1 IFN could be improved by the addition of anti-HCV enzymatic nucleic acid treatment, a dose response (0 U/ml to 100 U/ml) with IFN alfa 2a or

IFN alfa 2b was performed in HeLa cells in combination with 200 nM site 195 anti-HCV enzymatic nucleic acid (RPI 13919) or enzymatic nucleic acid control (SAC) treatment. The SAC control (RPI 17894) is a scrambled binding arm, attenuated core version of the site 195 enzymatic nucleic acid (RPI 13919). IFN dose responses were performed with different pretreatment regimes to find the dynamic range of inhibition in this system. In these studies, HeLa cells were used instead of HepG2 because of more efficient enzymatic nucleic acid delivery (Macejak *et al.*, 2000, *Hepatology*, 31, 769-776).

Cells and Virus

HeLa cells were maintained in DMEM (BioWhittaker, Walkersville, MD) supplemented with 5% fetal bovine serum. A cloned DNA copy of the HCV-PV chimeric virus was a gift of Dr. Eckard Wimmer (NYU, Stony Brook, NY). An RNA version was generated by in vitro transcription and transfected into HeLa cells to produce infectious virus (Lu and Wimmer, 1996, PNAS USA., 93, 1412-1417).

Enzymatic nucleic acid Synthesis

Nuclease resistant enzymatic nucleic acids and control oligonucleotides containing 2'-O-methyl-nucleotides, 2'-deoxy-2'-C-allyl uridine, a 3'-inverted abasic cap, and phosphorothioate linkages were chemically synthesized. The anti-HCV enzymatic nucleic acid (RPI 13919) targeting cleavage after nucleotide 195 of the 5' UTR of HCV is shown in **Table XX**. Attenuated core controls have nucleotide changes in the core sequence that greatly diminished the enzymatic nucleic acid's cleavage activity. The attenuated controls either contain scrambled binding arms (referred to as SAC, RPI 18743) or maintain binding arms (BAC, RPI 17894) capable of binding to the HCV RNA target.

Enzymatic nucleic acid Delivery

A cationic lipid was used as a cytofectin agent. HeLa cells were seeded in 96-well plates at a density of 9000-10,000 cells/well and incubated at 37°C under 5% CO₂ for 24 h. Transfection of enzymatic nucleic acid or control oligonucleotides (200 nM) was achieved by mixing 10X enzymatic nucleic acid or control oligonucleotides (2000 nM) with 10X RPI.9778 (80 µg/ml) in DMEM containing 5% fetal bovine serum (FBS) in U-bottom 96-well plates to make 5X complexes. Enzymatic nucleic acid/lipid complexes were allowed to incubate for 15 min at 37°C under 5% CO₂. Medium was aspirated from cells and replaced with 80 µl of DMEM (Gibco BRL) containing 5% FBS serum, followed by the addition of 20 µl of 5X complexes. Cells were incubated with complexes for 24 h at 37°C under 5% CO₂.

Interferon/Enzymatic nucleic acid Combination Treatment

Interferon alfa 2a (Roferon®) was purchased from Roche Bioscience (Palo Alto, CA). Interferon alfa 2b (Intron A®) was purchased from Schering-Plough Corporation (Madison, NJ). Consensus interferon (interferon-alfa-con 1) was a generous gift of Amgen, Inc. (Thousand Oaks, CA). For the basis of comparison, the manufacturers' specified units were used in the studies reported here; however, the manufacturers' unit definitions of these three IFN preparations are not necessarily the same. Nevertheless, since clinical dosing is based on the manufacturers' specified units, a direct comparison based on these units has relevance to clinical therapeutic indices. HeLa cells were seeded (10,000 cells per well) and incubated at 37°C under 5% CO₂ for 24 h. Cells were then pre-treated with interferon in complete media (DMEM + 5% FBS) for 4 h and then infected with HCV-PV at a multiplicity of infection (MOI) = 0.1 for 30 min. The viral inoculum was then removed and enzymatic nucleic acid or attenuated control (SAC or BAC) was delivered with the cytofectin formulation (8 µg/ml) in complete media for 24 h as described above. Where indicated for enzymatic nucleic acid dose response studies, active enzymatic nucleic acid was mixed with SAC to maintain a 200 nM total oligonucleotide concentration and the same lipid charge ratio. After 24 h, cells were lysed to release virus by three cycles of freeze/thaw. Virus was quantified by plaque assay and viral yield is reported as mean plaque forming units per ml (pfu/ml) + SD. All experiments were repeated at least twice and the trends in the results reported were reproducible. Significance levels (P values) were determined by the Student's test.

Plaque Assay

Virus samples were diluted in serum-free DMEM and 100 µl applied to Vero cell monolayers (~80% confluent) in 6-well plates for 30 min. Infected monolayers were overlaid with 3 ml 1.2% agar (Sigma Chemical Company, St. Louis, MO) and incubated at 37°C under 5% CO₂. When plaques were visible (after two to three days) the overlay was removed, monolayers were stained with 1.2% crystal violet, and plaque forming units were counted.

Results

As shown in **Figure 29A** and **29B**, treatment with the site 195 (RPI 13919) anti-HCV hammerhead enzymatic nucleic acid alone (0 U/ml IFN) resulted in viral replication that was dramatically reduced compared to SAC-treated cells (85%, $P < 0.01$). For both IFN alfa 2a (**Figure 29A**) or IFN alfa 2b (**Figure 29B**), treatment with 25 U/ml resulted in a ~90% inhibition of HCV-PV replication in SAC-treated cells as compared to cells treated with SAC alone ($p < 0.01$ for both observations). The maximal level of inhibition in SAC-treated cells (94%) was achieved by treatment with ≥ 50 U/ml of either IFN alfa 2a or IFN alfa 2b ($p < 0.01$ for both observations *versus* SAC alone). Maximal inhibition could however, be achieved by a 5-fold lower dose of IFN alfa 2a (10 U/ml) if enzymatic nucleic acid targeting site 195 in the 5' UTR of HCV RNA was given in combination (**Figure 29A**, $p < 0.01$). While the

additional effect of enzymatic nucleic acid treatment on IFN alfa 2b-treated cells at 10 U/ml was very slight, the combined effect with 25 U/ml IFN alfa 2b was greater in magnitude (**Figure 29B**). For both interferons tested, pretreatment with 25 U/ml in combination with 200 nM site 195 anti-HCV enzymatic nucleic acid resulted in an even greater level of inhibition of viral replication (>98%) compared to replication in cells treated with 200 nM SAC alone ($P<0.01$).

A dose response of the site 195 anti-HCV enzymatic nucleic acid was also performed in HeLa cells, either with or without 12.5 U/ml IFN alfa 2a or IFN alfa 2b pretreatment. As shown in **Figure 30**, enzymatic nucleic acid-mediated inhibition was dose-dependent and a significant inhibition of HCV-PV replication (>75% *versus* 0 nM enzymatic nucleic acid, $P<0.01$) could be achieved by treatment with ≥ 150 nM anti-HCV enzymatic nucleic acid alone (no IFN). However, in IFN-pretreated cells, the dose of anti-HCV enzymatic nucleic acid needed to achieve this level of inhibition was decreased 3-fold to 50 nM ($P<0.01$ *versus* 0 nM enzymatic nucleic acid). In comparison, treatment with the site 195 anti-HCV enzymatic nucleic acid alone at 50 nM resulted in only ~40% inhibition of virus replication. Pretreatment with IFN enhanced the antiviral effect of site 195 enzymatic nucleic acid at all enzymatic nucleic acid doses, compared to no IFN pretreatment.

Interferon-alfacon1, consensus IFN (CIFN), is another type 1 IFN that is used to treat chronic HCV. To determine if a similar enhancement can occur in CIFN-treated cells, a dose response with CIFN was performed in HeLa cells using 0 U/ml to 12.5 U/ml CIFN in combination with 200 nM site 195 anti-HCV enzymatic nucleic acid or SAC treatment (**Figure 31A**). Again, in the presence of the site 195 anti-HCV enzymatic nucleic acid alone, viral replication was dramatically reduced compared to SAC-treated cells. As shown in **Figure 31A**, treatment with 200 nM anti-HCV enzymatic nucleic acid alone significantly inhibited HCV-PV replication (90% *versus* SAC treatment, $P<0.01$). However, pretreatment with concentrations of CIFN from 1 U/ml to 12.5 U/ml in combination with 200 nM anti-HCV enzymatic nucleic acid resulted in even greater inhibition of viral replication (>98%) compared to replication in cells treated with 200 nM SAC alone ($P<0.01$). It is important to note that pretreatment with 1 U/ml CIFN in SAC-treated cells did not have a significant effect on HCV-poliovirus replication, but in the presence of enzymatic nucleic acid a significant inhibition of replication was observed (>98%, $P<0.01$). Thus, the dose of CIFN needed to achieve a >98% inhibition could be lowered to 1 U/ml in cells also treated with 200 nM site 195 anti-HCV enzymatic nucleic acid.

A dose response of site 195 anti-HCV enzymatic nucleic acid was then performed in HeLa cells, either with or without 12.5 U/ml CIFN pretreatment. As shown in **Figure 31B**, a significant inhibition of HCV-PV replication (>95% *versus* 0 nM enzymatic nucleic acid,

P<0.01) could be achieved by treatment with ≥ 150 nM anti-HCV enzymatic nucleic acid alone. However, in CIFN-pretreated cells, the dose of anti-HCV enzymatic nucleic acid needed to achieve this level of inhibition was only 50 nM (P<0.01). In comparison, treatment with the site 195 anti-HCV enzymatic nucleic acid alone at 50 nM resulted in ~50% inhibition of virus replication. Thus, as was seen with IFN alfa 2a and IFN alfa 2b, the dose of enzymatic nucleic acid could be reduced 3-fold in the presence of CIFN pretreatment to achieve a similar antiviral effect as enzymatic nucleic acid-treatment alone.

To further explore the combination of lower enzymatic nucleic acid concentration and CIFN, a dose response with 0 U/ml to 12.5 U/ml CIFN was subsequently performed in HeLa cells in combination with 50 nM site 195 anti-HCV enzymatic nucleic acid treatment. In multiple experiments, treatment with 50 nM anti-HCV enzymatic nucleic acid alone inhibited HCV-PV replication 50% – 81% compared to viral replication in SAC-treated cells. As for the experiment shown in **Figure 31A**, treatment with CIFN alone at 5 U/ml resulted in ~50% inhibition of viral replication. However, a four hour pretreatment with 5 U/ml CIFN followed by 50 nM anti-HCV enzymatic nucleic acid treatment resulted in 95% - 97% inhibition compared to SAC-treated cells (P<0.01).

To demonstrate that the enhanced antiviral effect of CIFN and enzymatic nucleic acid combination treatment was dependent upon enzymatic nucleic acid cleavage activity, the effect of CIFN in combination with site 195 anti-HCV enzymatic nucleic acid versus the effect of CIFN in combination with a binding competent, attenuated core, control (BAC) was then compared. The BAC can still bind to its specific RNA target, but is greatly diminished in cleavage activity. Pretreatment with 12.5 U/ml CIFN reduced the viral yield ~90% (7-fold) in cells treated with BAC (compare CIFN versus BAC in **Figure 32**). Cells treated with 200 nM site 195 anti-HCV enzymatic nucleic acid alone produced ~95% (17-fold) less virus than BAC-treated cells (195 RZ BAC in **Figure 32**). The combination of CIFN pretreatment and 200 nM site 195 anti-HCV enzymatic nucleic acid results in an augmented >98% (300-fold) reduction in viral yield (CIFN+RZ versus control in **Figure 32**).

2'-5'-Oligoadenylate Inhibition of HCV

Type 1 Interferon is a key constituent of many effective treatment programs for chronic HCV infection. Treatment with type 1 interferon induces a number of genes and results in an antiviral state within the cell. One of the genes induced is 2', 5' oligoadenylate synthetase, an enzyme that synthesizes short 2', 5' oligoadenylate (2-5A) molecules. Nascent 2-5A subsequently activates a latent RNase, RNase L, which in turn nonspecifically degrades viral RNA. As described herein, ribozymes targeting HCV RNA that inhibit the replication of an HCV-poliovirus (HCV-PV) chimera in cell culture and have shown that this antiviral effect is

augmented if ribozyme is given in combination with type 1 interferon. In addition, the 2-5A component of the interferon response can also inhibit replication of the HCV-PV chimera.

The antiviral effect of anti-HCV ribozyme treatment is enhanced if type 1 interferon is given in combination. Interferon induces a number of gene products including 2',5' oligoadenylate (2-5A) synthetase, double-stranded RNA-activated protein kinase (PKR), and the Mx proteins. Mx proteins appear to interfere with nuclear transport of viral complexes and are not thought to play an inhibitory role in HCV infection. On the other hand, the additional 2-5A-mediated RNA degradation (via RNase L) and/or the inhibition of viral translation by PKR in interferon-treated cells can augment the ribozyme-mediated inhibition of HCV-PV replication.

To investigate the potential role of the 2-5A/RNase L pathway in this enhancement phenomenon, HCV-PV replication was analyzed in HeLa cells treated exogenously with chemically-synthesized analogs of 2-5A (**Figure 35**), alone and in combination with the anti-HCV ribozyme (RPI 13919). These results were compared to replication in cells treated with interferon and/or anti-HCV ribozyme. Anti-HCV ribozyme was transfected into cells with a cationic lipid. To control for nonspecific effects due to lipid-mediated transfection, a scrambled arm, attenuated core, oligonucleotide (SAC) (RPI 17894) was transfected for comparison. The SAC is the same base composition as the ribozyme but is greatly attenuated in catalytic activity due to changes in the core sequence and cannot bind specifically to the HCV sequence.

As shown in **Figure 36A**, HeLa cells pretreated with 10 U/ml consensus interferon for 4 hours prior to HCV-PV infection resulted in ~70% reduction of viral replication in SAC-treated cells. Similarly, HeLa cells treated with 100 nM anti-HCV ribozyme for 20 hours after infection resulted in an ~80% reduction in viral yield. This antiviral effect was enhanced to ~98% inhibition in HeLa cells pretreated with interferon for 4 hours before infection and then treated with anti-HCV ribozyme for 20 hours after infection. In parallel, a 2-5A compound (analog I, **Figure 35**) that was protected from nuclease digestion at the 3'-end with an inverted abasic moiety was tested. As shown in **Figure 36B**, treatment with 200 nM 2-5A analog I for 4 hours prior to HCV-PV infection only slightly inhibited HCV-PV replication (~20%) in SAC-treated cells. Moreover, the inhibition due to a 20 hour anti-HCV ribozyme treatment was not augmented with a 4 hour pretreatment of 2-5A in combination (compare third bar to fourth bar in **Figure 36B**).

There are several possible explanations why the chemically synthesized 2-5A analog was not able to completely activate RNase L. It is possible that the 2-5A analog was not sufficiently stable or that in this experiment the 4 hour pretreatment period was too short for RNase L activation. To test these possibilities, a 2-5A compound containing a 5'-terminal

thiophosphate (P=S) for added nuclease resistance, in addition to the 3'- abasic, was also included (analog II, **Figure 35**). In addition, a longer 2-5A treatment was used. In this experiment (**Figure 37**), HeLa cells were treated with 2-5A or 2-5A(P=S) for 20 hours after HCV-PV infection. Again, anti-HCV ribozyme treatment resulted in >80% inhibition. In contrast to the 20% inhibition of viral replication seen with a 4 hour 2-5A pretreatment, viral replication in cells treated with 2-5A analog I for 20 hours after HCV-PV infection was inhibited by ~70%. The P=S version (analog II) inhibited HCV-PV replication by ~35%. Thus, both 2-5A analogs used here are able to generate an antiviral effect, presumably through RNase L activation. The P=S version, although more resistant to 5' dephosphorylation, did not yield as great an anti-viral effect. It is possible that combination of the 5'-terminal thiophosphate together with the presence of a 3'-inverted abasic moiety can interfere with RNase L activation. Nevertheless, these results demonstrate potent anti-HCV activity by a nuclease-stabilized 2-5A analog.

The level of reduction in HCV-PV replication in cells treated with 2-5A analog I for 20 hours was similar to that in cells pretreated with consensus interferon for 4 hours. To determine if this expanded 2-5A treatment regimen would enhance anti-HCV ribozyme efficacy to the same degree as does the interferon pretreatment, HeLa cells infected with HCV-PV were treated with a combination of 2-5A and anti-HCV ribozyme for 20 hours after infection. In this experiment, a 200 nM treatment with anti-HCV ribozyme or 2-5A treatment alone inhibited viral replication by 88% or ~60%, respectively, compared to SAC treatment (**Figure 38**, left three bars). To maintain consistent transfection conditions but vary the concentration of anti-HCV ribozyme or 2-5A, anti-HCV ribozyme was mixed with the SAC to maintain a total dose of 200 nM. A 50 nM treatment with anti-HCV ribozyme inhibited HCV-PV replication by ~70% (solid middle bar). However, the amount of HCV-PV replication was not further reduced in cells treated with a combination of 50 nM anti-HCV ribozyme and 150 nM 2-5A (striped middle bar). Likewise, cells treated with 100 nM anti-HCV ribozyme inhibited HCV-PV replication by ~80% whether they were also treated with 100 nM of 2-5A or SAC (right two bars). In contrast, antiviral activity increased from 80% to 98% when 100 nM anti-HCV ribozyme was given in combination with interferon (**Figure 36A**). The reasons for the lack of additive or synergistic effects for the ribozyme/2-5A combination therapy is unclear at this time but can be due to that fact that both compounds have a similar mechanism of action (degradation of RNA). Further study is warranted to examine this possibility.

As a monotherapy, 2-5A treatment generates a similar inhibitory effect on HCV-poliovirus replication as does interferon treatment. If these results are maintained in HCV patients, treatment with 2-5A can not only be efficacious but can also generate less side

effects than those observed with interferon if the plethora of interferon-induced genes were not activated.

HBV Cell Culture Models

As previously mentioned, HBV does not infect cells in culture. However, transfection of HBV DNA (either as a head-to-tail dimer or as an “overlength” genome of >100%) into HuH7 or Hep G2 hepatocytes results in viral gene expression and production of HBV virions released into the media. Thus, HBV replication competent DNA are co-transfected with ribozymes in cell culture. Such an approach has been used to report intracellular ribozyme activity against HBV (zu Putlitz, *et al.*, 1999, *J. Virol.*, 73, 5381-5387, and Kim *et al.*, 1999, *Biochem. Biophys. Res. Commun.*, 257, 759-765). In addition, stable hepatocyte cell lines have been generated that express HBV. In these cells, only ribozyme need be delivered; however, performance of a delivery screen is required. Intracellular HBV gene expression can be assayed by a Taqman® assay for HBV RNA or by ELISA for HBV protein. Extracellular virus can be assayed by PCR for DNA or ELISA for protein. Antibodies are commercially available for HBV surface antigen and core protein. A secreted alkaline phosphatase expression plasmid can be used to normalize for differences in transfection efficiency and sample recovery.

HBV Animal Models

There are several small animal models to study HBV replication. One is the transplantation of HBV-infected liver tissue into irradiated mice. Viremia (as evidenced by measuring HBV DNA by PCR) is first detected 8 days after transplantation and peaks between 18 – 25 days (Ilan *et al.*, 1999, *Hepatology*, 29, 553-562).

Transgenic mice that express HBV have also been used as a model to evaluate potential anti-virals. HBV DNA is detectable in both liver and serum (Guidotti *et al.*, 1995, *J. Virology*, 69, 10, 6158-6169; Morrey *et al.*, 1999, *Antiviral Res.*, 42, 97-108).

An additional model is to establish subcutaneous tumors in nude mice with Hep G2 cells transfected with HBV. Tumors develop in about 2 weeks after inoculation and express HBV surface and core antigens. HBV DNA and surface antigen is also detected in the circulation of tumor-bearing mice (Yao *et al.*, 1996, *J. Viral Hepat.*, 3, 19-22).

In one embodiment, the invention features a mouse, for example a male or female mouse, implanted with HepG2.2.15 cells, wherein the mouse is susceptible to HBV infection and capable of sustaining HBV DNA expression. One embodiment of the invention provides a mouse implanted with HepG2.2.15 cells, wherein said mouse sustains the propagation of

HEPG2.2.15 cells and HBV production (see Macejak, US Provisional Patent Application No. 60/296,876).

Woodchuck hepatitis virus (WHV) is closely related to HBV in its virus structure, genetic organization, and mechanism of replication. As with HBV in humans, persistent WHV infection is common in natural woodchuck populations and is associated with chronic hepatitis and hepatocellular carcinoma (HCC). Experimental studies have established that WHV causes HCC in woodchucks and woodchucks chronically infected with WHV have been used as a model to test a number of anti-viral agents. For example, the nucleoside analogue 3T3 was observed to cause dose dependent reduction in virus (50% reduction after two daily treatments at the highest dose) (Hurwitz *et al.*, 1998. *Antimicrob. Agents Chemother.*, 42, 2804-2809).

HCV Cell Culture Models

Although there have been reports of replication of HCV in cell culture (see below), these systems are difficult to replicate and have proven unreliable. Therefore, as was the case for development of other anti-HCV therapeutics such as interferon and ribavirin, after demonstration of safety in animal studies applicant can proceed directly into a clinical feasibility study.

Several recent reports have documented *in vitro* growth of HCV in human cell lines (Mizutani *et al.*, *Biochem Biophys Res Commun* 1996 227(3):822-826; Tagawa *et al.*, *Journal of Gastroenterology and Hepatology* 1995 10(5):523-527; Cribier *et al.*, *Journal of General Virology* 76(10):2485-2491; Seipp *et al.*, *Journal of General Virology* 1997 78(10):2467-2478; Iacovacci *et al.*, *Research Virology* 1997 148(2):147-151; Iacovacci *et al.*, *Hepatology* 1997 26(5) 1328-1337; Ito *et al.*, *Journal of General Virology* 1996 77(5):1043-1054; Nakajima *et al.*, *Journal of Virology* 1996 70(5):3325-3329; Mizutani *et al.*, *Journal of Virology* 1996 70(10):7219-7223; Valli *et al.*, *Res Virol* 1995 146(4): 285-288; Kato *et al.*, *Biochem Biophys Res Comm* 1995 206(3):863-869). Replication of HCV has been demonstrated in both T and B cell lines as well as cell lines derived from human hepatocytes. Demonstration of replication was documented using either RT-PCR based assays or the b-DNA assay. It is important to note that the most recent publications regarding HCV cell cultures document replication for up to 6-months.

Additionally, another recent study has identified more robust strains of hepatitis C virus having adaptive mutations that allow the strains to replicate more vigorously in human cell culture. The mutations that confer this enhanced ability to replicate are located in a specific region of a protein identified as NS5A. Studies performed at Rockefeller University have shown that in certain cell culture systems, infection with the robust strains produces a 10,000-

fold increase in the number of infected cells. The greatly increased availability of HCV-infected cells in culture can be used to develop high-throughput screening assays, in which a large number of compounds, such as enzymatic nucleic acid molecules, can be tested to determine their effectiveness.

5 In addition to cell lines that can be infected with HCV, several groups have reported the successful transformation of cell lines with cDNA clones of full-length or partial HCV genomes (Harada *et al.*, Journal of General Virology 1995 76(5):1215-1221; Haramatsu *et al.*, Journal of Viral Hepatitis 1997 4S(1):61-67; Dash *et al.*, American Journal of Pathology 1997 151(2):363-373; Mizuno *et al.*, Gastroenterology 1995 109(6):1933-40; Yoo *et al.*,
10 Journal Of Virology 1995 69(1):32-38).

HCV Animal Models

The best characterized animal system for HCV infection is the chimpanzee. Moreover, the chronic hepatitis that results from HCV infection in chimpanzees and humans is very similar. Although clinically relevant, the chimpanzee model suffers from several practical
15 impediments that make use of this model difficult. These include; high cost, long incubation requirements and lack of sufficient quantities of animals. Due to these factors, a number of groups have attempted to develop rodent models of chronic hepatitis C infection. While direct infection has not been possible several groups have reported on the stable transfection of either portions or entire HCV genomes into rodents (Yamamoto *et al.*, Hepatology 1995
20 22(3): 847-855; Galun *et al.*, Journal of Infectious Disease 1995 172(1):25-30; Koike *et al.*, Journal of general Virology 1995 76(12):3031-3038; Pasquinelli *et al.*, Hepatology 1997 25(3): 719-727; Hayashi *et al.*, Princess Takamatsu Symp 1995 25:1430149; Mariya K, Yotsuyanagi H, Shintani Y, Fujie H, Ishibashi K, Matsuura Y, Miyamura T, Koike K. Hepatitis C virus core protein induces hepatic steatosis in transgenic mice. Journal of General
25 Virology 1997 78(7) 1527-1531; Takehara *et al.*, Hepatology 1995 21(3):746-751; Kawamura *et al.*, Hepatology 1997 25(4): 1014-1021). In addition, transplantation of HCV infected human liver into immunocompromised mice results in prolonged detection of HCV RNA in the animal's blood.

Vierling, International PCT Publication No. WO 99/16307, describes a method for
30 expressing hepatitis C virus in an *in vivo* animal model. Viable, HCV infected human hepatocytes are transplanted into a liver parenchyma of a scid/scid mouse host. The scid/scid mouse host is then maintained in a viable state, whereby viable, morphologically intact human hepatocytes persist in the donor tissue and hepatitis C virus is replicated in the persisting human hepatocytes. This model provides an effective means for the study of HCV
35 inhibition by enzymatic nucleic acids *in vivo*.

Indications

Particular degenerative and disease states that can be associated with HBV expression modulation include, but are not limited to, HBV infection, hepatitis, cancer, tumorigenesis, cirrhosis, liver failure and other conditions related to the level of HBV.

- 5 Particular degenerative and disease states that can be associated with HCV expression modulation include, but are not limited to, HCV infection, hepatitis, cancer, tumorigenesis, cirrhosis, liver failure and other conditions related to the level of HCV.

- 10 The present body of knowledge in HBV and HCV research indicates the need for methods to assay HBV or HCV activity and for compounds that can regulate HBV and HCV expression for research, diagnostic, and therapeutic use.

- 15 Lamivudine (3TC®), L-FMAU, adefovir dipivoxil, type 1 Interferon (*e.g.*, interferon alpha, interferon beta, consensus interferon, polyethylene glycol interferon, polyethylene glycol interferon alpha 2a, polyethylene glycol interferon 2b, and polyethylene glycol consensus interferon), therapeutic vaccines, steroids, and 2'-5' Oligoadenylates are non-limiting examples of pharmaceutical agents that can be combined with or used in conjunction with the nucleic acid molecules (*e.g.* ribozymes and antisense molecules) of the instant invention. Those skilled in the art will recognize that other drugs or other therapies can similarly and readily be combined with the nucleic acid molecules of the instant invention (*e.g.* ribozymes and antisense molecules) and are, therefore, within the scope of the instant invention.
- 20

Diagnostic uses

- 25 The nucleic acid molecules of this invention can be used as diagnostic tools to examine genetic drift and mutations within diseased cells or to detect the presence of HBV or HCV RNA in a cell. For example, the close relationship between enzymatic nucleic acid activity and the structure of the target RNA allows the detection of mutations in any region of the molecule which alters the base-pairing and three-dimensional structure of the target RNA. By using multiple enzymatic nucleic acids described in this invention, one can map nucleotide changes which are important to RNA structure and function *in vitro*, as well as in cells and tissues. Cleavage of target RNAs with enzymatic nucleic acids can be used to
- 30 inhibit gene expression and define the role (essentially) of specified gene products in the progression of disease. In this manner, other genetic targets can be defined as important mediators of the disease. These experiments can lead to better treatment of the disease progression by affording the possibility of combinational therapies (*e.g.*, multiple enzymatic nucleic acid molecules targeted to different genes, enzymatic nucleic acid molecules coupled

with known small molecule inhibitors, or intermittent treatment with combinations of enzymatic nucleic acid molecules and/or other chemical or biological molecules). Other *in vitro* uses of enzymatic nucleic acid molecules of this invention are well known in the art, and include detection of the presence of mRNAs associated with HBV or HCV-related condition.

5 Such RNA is detected by determining the presence of a cleavage product after treatment with an enzymatic nucleic acid using standard methodology.

In a specific example, enzymatic nucleic acid molecules which can cleave only wild-type or mutant forms of the target RNA are used for the assay. The first enzymatic nucleic acid is used to identify wild-type RNA present in the sample and the second enzymatic
 10 nucleic acid is used to identify mutant RNA in the sample. As reaction controls, synthetic substrates of both wild-type and mutant RNA can be cleaved by both enzymatic nucleic acid molecules to demonstrate the relative ribozyme efficiencies in the reactions and the absence of cleavage of the “non-targeted” RNA species. The cleavage products from the synthetic substrates can also serve to generate size markers for the analysis of wild-type and mutant
 15 RNAs in the sample population. Thus each analysis involves two enzymatic nucleic acid molecules, two substrates and one unknown sample which is combined into six reactions. The presence of cleavage products is determined using an RNase protection assay so that full-length and cleavage fragments of each RNA can be analyzed in one lane of a polyacrylamide gel. It is not absolutely required to quantify the results to gain insight into
 20 the expression of mutant RNAs and putative risk of the desired phenotypic changes in target cells. The expression of mRNA whose protein product is implicated in the development of the phenotype (*i.e.*, HBV or HCV) is adequate to establish risk. If probes of comparable specific activity are used for both transcripts, then a qualitative comparison of RNA levels is adequate and will decrease the cost of the initial diagnosis. Higher mutant form to wild-type
 25 ratios are correlated with higher risk whether RNA levels are compared qualitatively or quantitatively.

Additional Uses

Potential usefulness of sequence-specific enzymatic nucleic acid molecules of the instant invention have many of the same applications for the study of RNA that DNA
 30 restriction endonucleases have for the study of DNA (Nathans *et al.*, 1975 *Ann. Rev. Biochem.* 44:273). For example, the pattern of restriction fragments can be used to establish sequence relationships between two related RNAs, and large RNAs can be specifically cleaved to fragments of a size more useful for study. The ability to engineer sequence specificity of the enzymatic nucleic acid molecule is ideal for cleavage of RNAs of unknown
 35 sequence. Applicant describes the use of nucleic acid molecules to down-regulate gene

expression of target genes in bacterial, microbial, fungal, viral, and eukaryotic systems including plant, or mammalian cells.

All patents and publications mentioned in the specification are indicative of the levels of skill of those skilled in the art to which the invention pertains. All references cited in this disclosure are incorporated by reference to the same extent as if each reference had been incorporated by reference in its entirety individually.

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The methods and compositions described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art, which are encompassed within the spirit of the invention, are defined by the scope of the claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. Thus, such additional embodiments are within the scope of the present invention and the following claims.

The invention illustratively described herein suitably can be practiced in the absence of any element or elements, limitation or limitations that are not specifically disclosed herein. Thus, for example, in each instance herein any of the terms “comprising”, “consisting essentially of” and “consisting of” may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments, optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the description and the appended claims.

In addition, where features or aspects of the invention are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush group or other group.

TABLE I

Characteristics of naturally occurring ribozymes

Group I Introns

- 5 • Size: ~150 to >1000 nucleotides.
- Requires a U in the target sequence immediately 5' of the cleavage site.
- Binds 4-6 nucleotides at the 5'-side of the cleavage site.
- Reaction mechanism: attack by the 3'-OH of guanosine to generate cleavage products with 3'-OH and 5'-guanosine.
- 10 • Additional protein cofactors required in some cases to help folding and maintenance of the active structure.
- Over 300 known members of this class. Found as an intervening sequence in *Tetrahymena thermophila* rRNA, fungal mitochondria, chloroplasts, phage T4, blue-green algae, and others.
- 15 • Major structural features largely established through phylogenetic comparisons, mutagenesis, and biochemical studies [i,ii].
- Complete kinetic framework established for one ribozyme [iii,iv,v,vi].
- Studies of ribozyme folding and substrate docking underway [vii,viii,ix].
- Chemical modification investigation of important residues well established [x,xi].
- 20 • The small (4-6 nt) binding site may make this ribozyme too non-specific for targeted RNA cleavage, however, the *Tetrahymena* group I intron has been used to repair a "defective" β -galactosidase message by the ligation of new β -galactosidase sequences onto the defective message [xii].

25 **RNAse P RNA (M1 RNA)**

- Size: ~290 to 400 nucleotides.
- RNA portion of a ubiquitous ribonucleoprotein enzyme.

- Cleaves tRNA precursors to form mature tRNA [xiii].
- Reaction mechanism: possible attack by M^{2+} -OH to generate cleavage products with 3'-OH and 5'-phosphate.
- 5 • RNase P is found throughout the prokaryotes and eukaryotes. The RNA subunit has been sequenced from bacteria, yeast, rodents, and primates.
- Recruitment of endogenous RNase P for therapeutic applications is possible through hybridization of an External Guide Sequence (EGS) to the target RNA [xiv,xv]
- Important phosphate and 2' OH contacts recently identified [xvi,xvii]

10 Group II Introns

- Size: >1000 nucleotides.
- Trans cleavage of target RNAs recently demonstrated [xviii,xix].
- Sequence requirements not fully determined.
- 15 • Reaction mechanism: 2'-OH of an internal adenosine generates cleavage products with 3'-OH and a "lariat" RNA containing a 3'-5' and a 2'-5' branch point.
- Only natural ribozyme with demonstrated participation in DNA cleavage [xx,xxi] in addition to RNA cleavage and ligation.
- Major structural features largely established through phylogenetic comparisons [xxii].
- 20 • Important 2' OH contacts beginning to be identified [xxiii]
- Kinetic framework under development [xxiv]

Neurospora VS RNA

- 25 • Size: ~144 nucleotides.
- Trans cleavage of hairpin target RNAs recently demonstrated [xxv].

- Sequence requirements not fully determined.
 - Reaction mechanism: attack by 2'-OH 5' to the scissile bond to generate cleavage products with 2',3'-cyclic phosphate and 5'-OH ends.
 - Binding sites and structural requirements not fully determined.
- 5 • Only 1 known member of this class. Found in *Neurospora* VS RNA.

Hammerhead Ribozyme

(see text for references)

- Size: ~13 to 40 nucleotides.
- 10 • Requires the target sequence UH immediately 5' of the cleavage site.
- Binds a variable number nucleotides on both sides of the cleavage site.
 - Reaction mechanism: attack by 2'-OH 5' to the scissile bond to generate cleavage products with 2',3'-cyclic phosphate and 5'-OH ends.
- 15 • 14 known members of this class. Found in a number of plant pathogens (virusoids) that use RNA as the infectious agent.
- Essential structural features largely defined, including 2 crystal structures [xxvi,xxvii]
 - Minimal ligation activity demonstrated (for engineering through *in vitro* selection) [xxviii]
 - Complete kinetic framework established for two or more ribozymes [xxix].
- 20 • Chemical modification investigation of important residues well established [xxx].

Hairpin Ribozyme

- Size: ~50 nucleotides.
- 25 • Requires the target sequence GUC immediately 3' of the cleavage site.

- Binds 4-6 nucleotides at the 5'-side of the cleavage site and a variable number to the 3'-side of the cleavage site.
- Reaction mechanism: attack by 2'-OH 5' to the scissile bond to generate cleavage products with 2',3'-cyclic phosphate and 5'-OH ends.
- 5 • 3 known members of this class. Found in three plant pathogen (satellite RNAs of the tobacco ringspot virus, arabis mosaic virus and chicory yellow mottle virus) which uses RNA as the infectious agent.
- Essential structural features largely defined [xxxi,xxxii,xxxiii,xxxiv]
- Ligation activity (in addition to cleavage activity) makes ribozyme amenable to
10 engineering through *in vitro* selection [xxxv]
- Complete kinetic framework established for one ribozyme [xxxvi].
- Chemical modification investigation of important residues begun [xxxvii,xxxviii].

Hepatitis Delta Virus (HDV) Ribozyme

15

- Size: ~60 nucleotides.
- Trans cleavage of target RNAs demonstrated [xxxix].
- Binding sites and structural requirements not fully determined, although no sequences 5' of cleavage site are required. Folded ribozyme contains a pseudoknot structure [xl].
- 20 • Reaction mechanism: attack by 2'-OH 5' to the scissile bond to generate cleavage products with 2',3'-cyclic phosphate and 5'-OH ends.
- Only 2 known members of this class. Found in human HDV.
- ^{xli}Circular form of HDV is active and shows increased nuclease stability [xlii]

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Table II:**A. 2.5 μ mol Synthesis Cycle ABI 394 Instrument**

Reagent	Equivalents	Amount	Wait Time* DNA	Wait Time* 2'-O-methyl	Wait Time*RNA
Phosphoramidites	6.5	163 μ L	45 sec	2.5 min	7.5 min
S-Ethyl Tetrazole	23.8	238 μ L	45 sec	2.5 min	7.5 min
Acetic Anhydride	100	233 μ L	5 sec	5 sec	5 sec
N-Methyl Imidazole	186	233 μ L	5 sec	5 sec	5 sec
TCA	176	2.3 mL	21 sec	21 sec	21 sec
Iodine	11.2	1.7 mL	45 sec	45 sec	45 sec
Beaucage	12.9	645 μ L	100 sec	300 sec	300 sec
Acetonitrile	NA	6.67 mL	NA	NA	NA

B. 0.2 μ mol Synthesis Cycle ABI 394 Instrument

Reagent	Equivalents	Amount	Wait Time* DNA	Wait Time* 2'-O-methyl	Wait Time*RNA
Phosphoramidites	15	31 μ L	45 sec	233 sec	465 sec
S-Ethyl Tetrazole	38.7	31 μ L	45 sec	233 min	465 sec
Acetic Anhydride	655	124 μ L	5 sec	5 sec	5 sec
N-Methyl Imidazole	1245	124 μ L	5 sec	5 sec	5 sec
TCA	700	732 μ L	10 sec	10 sec	10 sec
Iodine	20.6	244 μ L	15 sec	15 sec	15 sec
Beaucage	7.7	232 μ L	100 sec	300 sec	300 sec
Acetonitrile	NA	2.64 mL	NA	NA	NA

C. 0.2 μ mol Synthesis Cycle 96 well Instrument

Reagent	Equivalents:DNA/ 2'-O-methyl/Ribo	Amount: DNA/2'-O- methyl/Ribo	Wait Time* DNA	Wait Time* 2'-O- methyl	Wait Time* Ribo
Phosphoramidites	22/33/66	40/60/120 μ L	60 sec	180 sec	360sec
S-Ethyl Tetrazole	70/105/210	40/60/120 μ L	60 sec	180 min	360 sec
Acetic Anhydride	265/265/265	50/50/50 μ L	10 sec	10 sec	10 sec
N-Methyl Imidazole	502/502/502	50/50/50 μ L	10 sec	10 sec	10 sec
TCA	238/475/475	250/500/500 μ L	15 sec	15 sec	15 sec
Iodine	6.8/6.8/6.8	80/80/80 μ L	30 sec	30 sec	30 sec
Beaucage	34/51/51	80/120/120	100 sec	200 sec	200 sec
Acetonitrile	NA	1150/1150/1150 μ L	NA	NA	NA

- Wait time does not include contact time during delivery.

Table III: HBV Strains and Accession numbers

Accession Number	NAME
AF100308.1	AF100308 Hepatitis B virus strain 2-18, complete
AB026815.1	AB026815 Hepatitis B virus DNA, complete genome,
AB033559.1	AB033559 Hepatitis B virus DNA, complete genome,
AB033558.1	AB033558 Hepatitis B virus DNA, complete genome,
AB033557.1	AB033557 Hepatitis B virus DNA, complete genome,
AB033556.1	AB033556 Hepatitis B virus DNA, complete genome,
AB033555.1	AB033555 Hepatitis B virus DNA, complete genome,
AB033554.1	AB033554 Hepatitis B virus DNA, complete genome,
AB033553.1	AB033553 Hepatitis B virus DNA, complete genome,
AB033552.1	AB033552 Hepatitis B virus DNA, complete genome,
AB033551.1	AB033551 Hepatitis B virus DNA, complete genome,
AB033550.1	AB033550 Hepatitis B virus DNA, complete genome
AF143308.1	AF143308 Hepatitis B virus clone WB1254, complete
AF143307.1	AF143307 Hepatitis B virus clone RM518, complete
AF143306.1	AF143306 Hepatitis B virus clone RM517, complete
AF143305.1	AF143305 Hepatitis B virus clone RM501, complete
AF143304.1	AF143304 Hepatitis B virus clone HD319, complete
AF143303.1	AF143303 Hepatitis B virus clone HD1406, complete
AF143302.1	AF143302 Hepatitis B virus clone HD1402, complete
AF143301.1	AF143301 Hepatitis B virus clone BW1903, complete
AF143300.1	AF143300 Hepatitis B virus clone 7832-G4, complete
AF143299.1	AF143299 Hepatitis B virus clone 7744-G9, complete
AF143298.1	AF143298 Hepatitis B virus clone 7720-G8, complete
AB026814.1	AB026814 Hepatitis B virus DNA, complete genome,
AB026813.1	AB026813 Hepatitis B virus DNA, complete genome,
AB026812.1	AB026812 Hepatitis B virus DNA, complete genome,
AB026811.1	AB026811 Hepatitis B virus DNA, complete genome,
AJ131956.1	HBV131956 Hepatitis B virus complete genome,
AF151735.1	AF151735 Hepatitis B virus, complete genome
AF090842.1	AF090842 Hepatitis B virus strain G5.27295, complete
AF090841.1	AF090841 Hepatitis B virus strain G4.27241, complete
AF090840.1	AF090840 Hepatitis B virus strain G3.27270, complete
AF090839.1	AF090839 Hepatitis B virus strain G2.27246, complete
AF090838.1	AF090838 Hepatitis B virus strain P1.27239, complete
Y18858.1	HBV18858 Hepatitis B virus complete genome, isolate
Y18857.1	HBV18857 Hepatitis B virus complete genome, isolate
D12980.1	HPBCG Hepatitis B virus subtype adr(SRADR) DNA,
Y18856.1	HBV18856 Hepatitis B virus complete genome, isolate
Y18855.1	HBV18855 Hepatitis B virus complete genome, isolate
AJ131133.1	HBV131133 Hepatitis B virus, complete genome, strain
X80925.1	HBVP6PCXX Hepatitis B virus (patient 6) complete
X80926.1	HBVP5PCXX Hepatitis B virus (patient 5) complete
X80924.1	HBVP4PCXX Hepatitis B virus (patient 4) complete

AF100309.1	Hepatitis B virus strain 56, complete genome
AF068756.1	AF068756 Hepatitis B virus, complete genome
AF043593.1	AF043593 Hepatitis B virus isolate 6/89, complete
Y07587.1	HBVAYWGEN Hepatitis B virus, complete genome
D28880.1	D28880 Hepatitis B virus DNA, complete genome, strain
X98076.1	HBVDEFVP3 Hepatitis B virus complete genome with
X98075.1	HBVDEFVP2 Hepatitis B virus complete genome with
X98074.1	HBVDEFVP1 Hepatitis B virus complete genome with
X98077.1	HBVCGWITY Hepatitis B virus complete genome, wild type
X98072.1	HBVCGINSC Hepatitis B virus complete genome with
X98073.1	HBVCGINCX Hepatitis B virus complete genome with
U95551.1	U95551 Hepatitis B virus subtype ayw, complete genome
D23684.1	HPBC6T588 Hepatitis B virus (C6-TKB588) complete genome
D23683.1	HPBC5SHK02 Hepatitis B virus (C5-HBVK02) complete genome
D23682.1	HPBB5SHK01 Hepatitis B virus (B5-HBVK01) complete genome
D23681.1	HPBC4HST2 Hepatitis B virus (C4-HBVST2) complete genome
D23680.1	HPBB4HST1 Hepatitis B virus (B4-HBVST1) complete genome
D00331.1	HPBADW3 Hepatitis B virus genome, complete genome
D00330.1	HPBADW2 Hepatitis B virus genome, complete genome
D50489.1	HPBA11A Hepatitis B virus DNA, complete genome
D23679.1	HPBA3HMS2 Hepatitis B virus (A3-HBVMS2) complete genome
D23678.1	HPBA2HYS2 Hepatitis B virus (A2-HBVYS2) complete genome
D23677.1	HPBA1HKK2 Hepatitis B virus (A1-HBVKK2) complete genome
D16665.1	HPBADRM Hepatitis B virus DNA, complete genome
D00329.1	HPBADW1 Hepatitis B virus (HBV) genome, complete genome
X97851.1	HBVP6CSX Hepatitis B virus (patient 6) complete genome
X97850.1	HBVP4CSX Hepatitis B virus (patient 4) complete genome
X97849.1	HBVP3CSX Hepatitis B virus (patient 3) complete genome
X97848.1	HBVP2CSX Hepatitis B virus (patient 2) complete genome
X51970.1	HVHEPB Hepatitis B virus (HBV 991) complete genome
M38636.1	HPBCGADR Hepatitis B virus, subtype adr, complete genome
X59795.1	HBVAYWMCG Hepatitis B virus (ayw subtype mutant)
M38454.1	HPBADR1CG Hepatitis B virus , complete genome
M32138.1	HPBHBVAA Hepatitis B virus variant HBV-alpha1, complete
J02203.1	HPBAYW Human hepatitis B virus (subtype ayw), complete
M12906.1	HPBADRA Hepatitis B virus subtype adr, complete genome
M54923.1	HPBADWZ Hepatitis B virus (subtype adw), complete genome
L27106.1	HPBMUT Hepatitis B virus mutant complete genome

Table IV: HBV Substrate Sequence

NT Position*	SUBSTRATE	SEQ ID
82	CUAUCGUCCCCUUCUUAUC	1.
101	CUACCGUCCGGCC	2.
159	CUUCUCAUCU	3.
184	CUUCCCUUACCAC	4.
269	GACUCUCAGAAUGUCAACGAC	5.
381	CUGUAGGCAUAAAUGGUCUG	6.
401	GUUCACCAGCACCAUGCAACUUUUU	7.
424	UUUCACGUCUGCCUAAUCAUC	8.
524	AUUUGGAGCUUC	9.
562	CUGACUUCUUCCUUCUAUUC	10.
649	CUCACCAUACCGCACUCA	11.
667	GGCAAGCUAUUCUGUG	12.
717	GGAAGUAAUUUGGAAGAC	13.
758	CAGCUAUGUCA AUGUUA	14.
783	CUAAAUAUCGGCCUAAAUCAGAC	15.
812	CAUUUCCUGUCUCACUUUUGGAAGAG	16.
887	UCCUGCUUACAGAC	17.
922	CAACACUCCGGAAACUACUGUUGUUAG	18.
989	CUCGCCUCGCAGACGAAGGUCUC	19.
1009	CAAUCGCCGCGUCGCAGAAG	20.
1031	AUCUCAAUUCUGGGAAUCUCA	21.
1052	AUGUUAGUAUCCCUUGGACUC	22.
1072	CAUAAGGUGGGAAACUUUACUG	23.
1109	CUGUACCUAUUCUUUAAAUCC	24.
1127	CUGAGUGGCAAACUCCC	25.
1271	CCAAUAUUCUGCCCUUGGACAA	26.
1297	AUUAACCAUAUUAUCCUGAACA	27.
1319	AUGCAGUUAUCAUUACUCAAACUA	28.
1340	AAACUAGGCAUUA	29.
1370	AGGCGGGCAUUCUAUAUAAGAGAG	30.
1393	GAAACUACGCGCAGCGCCUCAUUUUGU	31.
1412	CAUUUUGUGGGUCACCAUA	32.
1441	CAAGAGCUACAGCAUGGG	33.

LOCUS HPBADR1CG 3221 bp DNA circular VRL
06-MAR-1995
DEFINITION Hepatitis B virus , complete genome.
ACCESSION M38454

*The nucleotide number referred to in that table is the position of the 5' end of the oligo in this sequence.

TABLE V: HUMAN HBV HAMMERHEAD RIBOZYME AND TARGET SEQUENCE

Pos	Substrate	Seq ID	Hammerhead	Seq ID
13	CCACCACU U UCCACCAA	34	UUGGUGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUGGUGG	7434
14	CACCACUU U CCACCAA	35	UUUGGUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAGUGGUG	7435
15	ACCACUUU C CACCAAAC	36	GUUUGGUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAAGUGGU	7436
25	ACCAACU C UUCAAGAU	37	AUCUUGAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUUUGGU	7437
27	CAAACUCU U CAAGAUC	38	GGAUCUUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGAGUUUG	7438
28	AAACUCUU C AAGAUC	39	GGGAUCUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAGAUUUU	7439
34	UUCAAGAU C CCAGAGUC	40	GACUCUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUCUUGAA	7440
42	CCCAGAGU C AGGGCCCU	41	AGGGCCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACUCUGGG	7441
53	GGCCUGU A CUUCCUG	42	CAGGAAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACAGGGCC	7442
56	CCUGUACU U UCCUGCUG	43	CAGCAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUACAGG	7443
57	CUGUACUU U CCUGCUGG	44	CCAGCAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAGUACAG	7444
58	UGUACUUU C CUGCUGGU	45	ACCAGCAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAAGUACA	7445
71	UGGUGGCU C CAGUUCAG	46	CUGAACUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGCCACCA	7446
76	GCUCCAGU U CAGGAACA	47	UGUUCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACUGGAGC	7447
77	CUCCAGUU C AGGAACAG	48	CUGUCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AACUGGAG	7448
97	GCCCUGCU C AGAAUACU	49	AGUAUUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGCAGGGC	7449
103	CUCAGAAU A CUGUCUCU	50	AGAGACAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUUCUGAG	7450
108	AAUACUGU C UCUGCCAU	51	AUGGCAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACAGUAUU	7451
110	UACUGUCU C UGCCAUU	52	AUAUGGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGACAGUA	7452
117	UCUGCCAU A UCGUCAAU	53	AUUGACGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUGGCAGA	7453
119	UGCCAUU C GUCAAUCU	54	AGAUUGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUAUGGCA	7454
122	CAUAUCGU C AAUCUUAU	55	AUAAGAUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACGAUUUG	7455
126	UCGUCAAU C UUAUCGAA	56	UUCGAUAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUUGACCA	7456
128	GUCAAUCU U AUCGAAGA	57	UCUUCGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGAUUGAC	7457
129	UCAAUUCU A UCGAAGAC	58	GUCUUCGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAGAUGUA	7458
131	AAUCUUAU C GAAGACUG	59	CAGUCUUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUAAGAUU	7459
150	GACCCUGU A CCGAACAU	60	AUGUUCGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACAGGGUC	7460
168	GAGAACAU C GCAUCAGG	61	CCUGAUGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUGUUCUC	7461
173	CAUCGCAU C AGGACUCC	62	GGAGUCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUGCGAUG	7462
180	UCAGGACU C CUAGGACC	63	GGUCCUAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUCCUGA	7463
183	GGACUCCU A GGACCCCU	64	AGGGGUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGGAGUCC	7464
195	CCCCUGCU C GUGUUAUA	65	UGUAACAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGCAGGGG	7465
200	GCUCGUGU U ACAGGCGG	66	CCGCCUGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACACGAGC	7466
201	CUCGUGUU A CAGGCGGG	67	CCCGCCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AACACGAG	7467
212	GGCGGGGU U UUUCUUGU	68	ACAAGAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACCCCGCC	7468
213	GCGGGGUU U UUCUUGUU	69	AACAAGAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AACCCCGC	7469
214	CGGGGUUU U UCUUGUUG	70	CAACAAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAACCCCG	7470
215	GGGGUUUU U CUUGUUGA	71	UCAACAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAAACCCC	7471
216	GGGUUUUU C UUGUUGAC	72	GUCAACAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAAAACCC	7472
218	GUUUUUCU U GUUGACAA	73	UUGUCAAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGAAAAAC	7473
221	UUUCUUGU U GACAAAAA	74	UUUUUGUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACAAGAAA	7474
231	ACAAAAAU C CUCACAAU	75	AUUGUGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUUUUUGU	7475
234	AAAAUCCU C ACAAUACC	76	GGUAUUGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGGAUUUU	7476
240	CUCACAAU A CCACAGAG	77	CUCUGUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUUGUGAG	7477
250	CACAGAGU C UAGACUCG	78	CGAGUCUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ACUCUGUG	7478
252	CAGAGUCU A GACUCGUG	79	CACGAGUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGACUCUG	7479

257	UCUAGACU C GUGGUGGA	80	UCCACCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCUAGA	7480
268	GGUGGACU U CUCUCAAU	81	AUUGAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCACC	7481
269	GUGGACUU C UCUCAAUU	82	AAUUGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUCCAC	7482
271	GGACUUCU C UCAAUUUU	83	AAAAUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGUCC	7483
273	ACUUCUCU C AAUUUUCU	84	AGAAAAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGAAGU	7484
277	CUCUCAAU U UUCUAGGG	85	CCCUAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGAGAG	7485
278	UCUCAAUU U UCUAGGGG	86	CCCCUAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGAGA	7486
279	CUCAAUUU U CUAGGGGG	87	CCCCCUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUUGAG	7487
280	UCAAUUUU C UAGGGGGA	88	UCCCCCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAUUGA	7488
282	AAUUUUCU A GGGGGAAC	89	GUUCCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAAAUU	7489
301	CCGUGUGU C UUGGCCAA	90	UUGGCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACACGG	7490
303	GUGUGUCU U GGCCAAAA	91	UUUUGGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACACAC	7491
313	GCCAAAAU U CGCAGUCC	92	GGACUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUGGC	7492
314	CCAAAAUU C GCAGUCCC	93	GGGACUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUUUGG	7493
320	UUCGCAGU C CCAAUUCU	94	AGAUUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGCGAA	7494
327	UCCCAAAU C UCCAGUCA	95	UGACUGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUGGA	7495
329	CCAAUUCU C CAGUCACU	96	AGUGACUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUUUGG	7496
334	UCUCCAGU C ACUCACCA	97	UGGUGAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGGAGA	7497
338	CAGUCACU C ACCAACCU	98	AGGUUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGACUG	7498
349	CAACCUGU U GUCCUCCA	99	UGGAGGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGGUUG	7499
352	CCUGUUGU C CUCCAUAU	100	AAUUGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAACAGG	7500
355	GUUGUCCU C CAAUUUGU	101	ACAAAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGACAAC	7501
360	CCUCCAAU U UGUCCUGG	102	CCAGGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGGAGG	7502
361	CUCCAUAU U GUCCUGGU	103	ACCAGGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGGAG	7503
364	CAAUUUGU C CUGGUUAU	104	AUAACCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAUUG	7504
370	GUCCUGGU U AUCGUGG	105	CCAGCGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCAGGAC	7505
371	UCCUGGUU A UCGUGGA	106	UCCAGCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCAGGA	7506
373	CUGGUUAU C GCUGGAUG	107	CAUCCAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAACCAG	7507
385	GGAUGUGU C UGCGGCGU	108	ACGCCGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACAUC	7508
394	UGCGGCGU U UUAUCAUC	109	GAUGAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGCCGCA	7509
395	GCGGCGUU U UAUCAUCU	110	AGAUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACGCCGC	7510
396	CGGCGUUU U AUAUCUU	111	AAGAUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACGCC	7511
397	GGCGUUUU A UCAUCUUC	112	GAAGAUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAACGCC	7512
399	CGUUUUUA C AUCUCCU	113	AGGAAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUAACG	7513
402	UUUAUCAU C UUCUCUG	114	CAGAGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUAAA	7514
404	UAUCAUCU U CCUCUGCA	115	UGCAGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUGAUA	7515
405	AUCAUCUU C CUCUGCAU	116	AUGCAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAUGAU	7516
408	AUCUCCU C UGCAUCCU	117	AGGAUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAAGAU	7517
414	CUCUGCAU C CUGCUGCU	118	AGCAGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCAGAG	7518
423	CUGCUGCU A UGCCUCAU	119	AUGAGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGCAG	7519
429	CUAUGCCU C AUCUUCUU	120	AAGAAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCAUAG	7520
432	UGCCUCAU C UUCUUGUU	121	AACAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAGGCA	7521
434	CCUCAUCU U CUUGUUGG	122	CCAACAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUGAGG	7522
435	CUCAUCUU C UUGUUGGU	123	ACCAACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAUGAG	7523
437	CAUCUUCU U GUUGGUUC	124	GAACCAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGAUG	7524
440	CUUCUUGU U GGUUCUUC	125	GAAGAACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAGAAG	7525
444	UUGUUGGU U CUUCUGGA	126	UCCAGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCAACAA	7526
445	UGUUGGUU C UUCUGGAC	127	GUCCAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCAACA	7527
447	UUGGUUCU U CUGGACUA	128	UAGUCCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAACCAA	7528
448	UGGUUCUU C UGGACUAU	129	AUAGUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAACCA	7529
455	UCUGGACU A UCAAGGUA	130	UACCUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCAGA	7530

457	UGGACUAU C AAGGUAUG	131	CAUACCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGUCCA	7531
463	AUCAAGGU A UGUUGCCC	132	GGGCAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUUGAU	7532
467	AGGUAUGU U GCCCUGUU	133	AAACGGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUACCU	7533
474	UUGCCCUGU U UGUCCUCU	134	AGAGGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGGCAA	7534
475	UGCCCUGU U GUCCUCUA	135	UAGAGGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACGGGCA	7535
478	CCGUUUGU C CUCUAAU	136	AAUUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAACGG	7536
481	UUUGUCCU C UAAUUGCA	137	UGGAAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGACAAA	7537
483	UGUCCUCU A AUUCCAGG	138	CCUGGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGGACA	7538
486	CCUCUAU U CCAGGAUC	139	GAUCCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAGAGG	7539
487	CUCUAAU C CAGGAUCA	140	UGAUCCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGAG	7540
494	UCCAGGAU C AACAACAA	141	UUGUUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCUGGA	7541
497	AGGAUCAU C AACAACCA	142	UGGUUGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUCCU	7542
535	GCACAACU C CUGCUCAA	143	UUGAGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUGUGC	7543
541	CUCCUGCU C AAGGAACC	144	GGUCCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGGAG	7544
551	AGGAACCU C UAUGUUUC	145	GAAACAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUCCU	7545
553	GAACCUCU A UGUUUCU	146	GGGAAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGGUUC	7546
557	CUCUAUGU U UCCCUCAU	147	AUGAGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUAGAG	7547
558	UCUAUGUU U CCCUCAUG	148	CAUGAGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAUAGA	7548
559	CUAUGUUU C CCUCAUGU	149	ACAUGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACAUAG	7549
563	GUUUCUCCU C AUGUUGCU	150	AGCAACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGAAAC	7550
568	CCUCAUGU U GCUGUACA	151	UGUACAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUGAGG	7551
574	GUUGCUGU A CAAAACCU	152	AGGUUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGCAAC	7552
583	CAAAACCU A CGGACGGA	153	UCCGUCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUUUG	7553
604	GCACCUGU A UUCCCAUC	154	GAUGGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGGUUC	7554
606	ACCUGUAU U CCCAUCCC	155	GGGAUGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACAGGU	7555
607	CCUGUAU C CCAUCCCA	156	UGGGAUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUACAGG	7556
612	AUUCUCCAU C CCAUCAUC	157	GAUGAUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGGAAU	7557
617	CAUCCCAU C AUCUUGGG	158	CCCAAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGGAUG	7558
620	CCCAUCAU C UUGGGCUU	159	AAGCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUGGG	7559
622	CAUCAUGU U GGGCUUUC	160	GAAAGCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUGAUG	7560
628	CUUGGGCU U UCGCAAAA	161	UUUUGCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCCAAG	7561
629	UUGGGCUU U CGCAAAAU	162	AUUUUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCCAA	7562
630	UGGGCUUU C GCAAAUA	163	UAUUUUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCCCA	7563
638	CGCAAAAU A CCUAUGGG	164	CCCAUAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUGCG	7564
642	AAAUACCU A UGGGAGUG	165	CACUCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUUUU	7565
656	GUGGGCCU C AGUCCGUU	166	AACGGACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCAC	7566
660	GCCUCAGU C CGUUUCUC	167	GAGAAACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGAGGC	7567
664	CAGUCCGU U UCUCUUGG	168	CCAAGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGACUG	7568
665	AGUCCGUU U CUCUUGGC	169	GCCAAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACGGACU	7569
666	GUCCGUUU C UCUUGGCU	170	AGCCAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACGGAC	7570
668	CCGUUUCU C UUGGCUCA	171	UGAGCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAACGG	7571
670	GUUUCUCU U GGCUCAGU	172	ACUGAGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGAAAC	7572
675	UCUUGGCU C AGUUUACU	173	AGUAAACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCAAGA	7573
679	GGCUCAGU U UACUAGUG	174	CACUAGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGAGCC	7574
680	GCUCAGUU U ACUAGUGC	175	GCACUAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACUGAGC	7575
681	CUCAGUUU A CUAGUGCC	176	GGCACUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACUGAG	7576
684	AGUUUACU A GUGCCAUU	177	AAUGGCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAAACU	7577
692	AGUGCCAU U UGUUCAGU	178	ACUGAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGCACU	7578
693	GUGCCAUU U GUUCAGUG	179	CACUGAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGGCAC	7579
696	CCAUUUGU U CAGUGGUU	180	AACCACUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAUUGG	7580
697	CAUUUGUU C AGUGGUUC	181	GAACCACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAAAUG	7581

704	UCAGUGGU U CGUAGGGC	182	GCCCUACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCACUGA	7582
705	CAGUGGUU C GUAGGGCU	183	AGCCCUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCACUG	7583
708	UGGUUCGU A GGGCUUUC	184	GAAAGCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGAACCA	7584
714	GUAGGGCU U UCCCCAC	185	GUGGGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCCUAC	7585
715	UAGGGCUU U CCCCCACU	186	AGUGGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCCUA	7586
716	AGGGCUUU C CCCCCACU	187	CAGUGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCCCU	7587
726	CCCACUGU C UGGCUUUC	188	GAAAGCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGUGGG	7588
732	GUCUGGCU U UCAGUUAU	189	AUAACUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCAGAC	7589
733	UCUGGCUU U CAGUUAUA	190	UAUAACUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCAGA	7590
734	CUGGCUUU C AGUUAUAU	191	AUAUAACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCCAG	7591
738	CUUUCAGU U AUAUGGAU	192	AUCCAUAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGAAAG	7592
739	UUUCAGUU A UAUGGAUG	193	CAUCCAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACUGAAA	7593
741	UCAGUUAU A UGGAUGAU	194	AUCAUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAACUGA	7594
755	GAUGUGGU U UUGGGGGC	195	GCCCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCACAUC	7595
756	AUGUGGUU U UGGGGGCC	196	GGCCCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCACAU	7596
757	UGUGGUUU U GGGGGCCA	197	UGCCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACCACA	7597
769	GGCCAAGU C UGUACAAC	198	GUUGUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUUGGCC	7598
773	AAGUCUGU A CAACAUCU	199	AGAUGUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGACUU	7599
780	UACAACAU C UUGAGUCC	200	GGACUCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUUGUA	7600
782	CAACAUCU U GAGUCCCU	201	AGGGACUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUGUUG	7601
787	UCUUGAGU C CCUUUAUG	202	CAUAAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCAAGA	7602
791	GAGUCCCU U UAUGCCGC	203	GCGGCAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGACUC	7603
792	AGUCCCUU U AUGCCGCU	204	AGCGGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGGACU	7604
793	GUCCCUUU A UGCCGCGU	205	CAGCGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGGGAC	7605
803	GCCGCGUU U ACCAAUUU	206	AAAUUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGCGGC	7606
804	CCGCGUUU A CCAAUUUU	207	AAAAUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAGCGG	7607
810	UUACCAAU U UUCUUUUG	208	CAAAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGGUAA	7608
811	UACCAAUU U UCUUUUGU	209	ACAAAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGGUA	7609
812	ACCAAUUU U CUUUUGUC	210	GACAAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUUGGU	7610
813	CCAAUUUU C UUUUGUCU	211	AGACAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAUUGG	7611
815	AAUUUUUC U UUGUCUUU	212	AAAGACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAAAUU	7612
816	AUUUUUCU U UGUCUUUG	213	CAAAGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAAAAU	7613
817	UUUUUCUU U GUCUUUGG	214	CCAAAGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAAAA	7614
820	UCUUUUGU C UUUGGGUA	215	UACCCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAAAAG	7615
822	UUUUGUCU U UGGGUUAU	216	UAUACCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACAAAA	7616
823	UUUGUCUU U GGGUAUAC	217	GUUAACCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACAAA	7617
828	CUUUGGGU A UACAUUUA	218	UAAAUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCCAAAG	7618
830	UUGGGUAU A CAUUUAAA	219	UUUAAAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACCCAA	7619
834	GUUAACAU U UAAACCCU	220	AGGGUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUAUAC	7620
835	UAUACAUU U AAACCCUC	221	GAGGGUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGUAUA	7621
836	AUACAUUU A AACCUCUA	222	UGAGGGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUGUAU	7622
843	UAAACCCU C ACAAACA	223	UGUUUUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGUUUA	7623
865	AUGGGGAU A UUCCCUUA	224	UAAGGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCCAU	7624
867	GGGGAUUA U CCCUUAAC	225	GUUAAGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUCCCC	7625
868	GGGAUUAU C CCUUAACU	226	AGUUAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUCCC	7626
872	UAUUCCCU U AACUUCAU	227	AUGAAGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGAAUA	7627
873	AUUCCCUU A ACUUCAUG	228	CAUGAAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGGAAU	7628
877	CCUUAACU U CAUGGGAU	229	AUCCCAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUAAGG	7629
878	CUUAACUU C AUGGGAUA	230	UAUCCCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUUAAG	7630
886	CAUGGGAU A UGUAAUUG	231	CAAUUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCCAUG	7631
890	GGAUAUGU A AUUGGGAG	232	CUCCCAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUAUCC	7632

893	UAUGUAAU U GGGAGUUG	233	CAACUCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUACAUA	7633
900	UUGGGAGU U GGGGCACA	234	UGUGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCCCAA	7634
910	GGGCACAU U GCCACAGG	235	CCUGUGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUGCCC	7635
924	AGGAACAU A UUGUACAA	236	UUGUACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCCU	7636
926	GAACAUAU U GUACAAAA	237	UUUUGUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUGUUC	7637
929	CAUAUUGU A CAAAAAU	238	AUUUUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUAUUG	7638
938	CAAAAAU C AAAAUGUG	239	CACAUUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUUUG	7639
948	AAAUGUGU U UUAGGAAA	240	UUUCCUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACAUUU	7640
949	AAUGUGUU U UAGGAAAC	241	GUUUCCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACACAUU	7641
950	AUGUGUUU A AGGAAACU	242	AGUUUCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACACAU	7642
951	UGUGUUUU A GGAAACUU	243	AAGUUUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAACACA	7643
959	AGGAAACU U CCUGUAAA	244	UUUACAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUUCCU	7644
960	GGAAACUU C CUGUAAAC	245	GUUUACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUUUCC	7645
965	CUUCCUGU A AACAGGCC	246	GGCCUGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGGAAG	7646
975	ACAGGCCU A UUGAUUGG	247	CCAAUCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCUGU	7647
977	AGGCCUUA U GAUUGGAA	248	UUCCAAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGGCCU	7648
981	CUAUUGAU U GGAAAGUA	249	UACUUUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCAAUAG	7649
989	UGGAAAGU A UGUCAACG	250	CGUUGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUUUCCA	7650
993	AAGUAUGU C AACGAAUU	251	AAUUCGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUACUU	7651
1001	CAACGAU U GUGGGUCU	252	AGACCCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCGUUG	7652
1008	UUGUGGGU C UUUUGGGG	253	CCCCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCACAA	7653
1010	GUGGGUCU U UUGGGGUU	254	AACCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCCAC	7654
1011	UGGGUCUU U UGGGGUUU	255	AAACCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACCCA	7655
1012	GGGUCUUU U GGGGUUUG	256	CAAACCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGACCC	7656
1018	UUUGGGGU U UGCCGCC	257	GGGCGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCCCAAA	7657
1019	UUGGGGUU U GCCGCCCC	258	GGGGCGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCCCAA	7658
1029	CCGCCCUU U UCACGCAA	259	UUGCGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGCGG	7659
1030	CGCCCCUU U CACGCAAU	260	AUUGCGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGGGCG	7660
1031	GCCCCUUU C ACGCAAUG	261	CAUUGCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGGGGC	7661
1045	AUGUGGAU A UUCUGCUU	262	AAGCAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCACAU	7662
1047	GUGGAUUA U CUGCUUUA	263	UAAAGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUCCAC	7663
1048	UGGAUAUU C UGCUUUA	264	UUAAAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUCCA	7664
1053	AUUCUGCU U UAAUGCCU	265	AGGCAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGAAU	7665
1054	UUCUGCUU U AAUGCCUU	266	AAGGCAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCAGAA	7666
1055	UCUGCUUU A AUGCCUUU	267	AAAGGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCAGA	7667
1062	UAAUGCCU U UAUAUGCA	268	UGCAUAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCAUUA	7668
1063	AAUGCCUU U AUAUGCAU	269	AUGCAUAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGCAUU	7669
1064	AUGCCUUU A UAUGCAUG	270	CAUGCAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGGCAU	7670
1066	GCCUUUAU A UGCAUGCA	271	UGCAUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAAGGC	7671
1076	GCAUGCAU A CAAGCAA	272	UUUGCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCAUGC	7672
1092	AACAGGCU U UUACUUUC	273	GAAAGUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCUGUU	7673
1093	ACAGGCUU U UACUUUCU	274	AGAAAGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCUGU	7674
1094	CAGGCUUU U ACUUUCUC	275	GAGAAAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCCUG	7675
1095	AGGCUUUU A CUUUCUCG	276	CGAGAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAGCCU	7676
1098	CUUUUACU U UCUCGCCA	277	UGGCGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAAAAG	7677
1099	UUUUACUU U CUCGCCAA	278	UUGGCGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUAAAA	7678
1100	UUUACUUU C UCGCCAAC	279	GUUGGCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGUAAA	7679
1102	UACUUUCU C GCCAACUU	280	AAGUUGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAAGUA	7680
1110	CGCCAACU U ACAAGGCC	281	GGCCUUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUGGCG	7681
1111	GCCAACUU A CAAGCCU	282	AGGCCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUUGGC	7682
1120	CAAGGCCU U UCUAAGUA	283	UACUAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCUUG	7683

1121	AAGGCCUU U CUAAGUAA	284	UUACUUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGCCUU	7684
1122	AGGCCUUU C UAAGUAAA	285	UUUACUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGGCCU	7685
1124	GCCUUUCU A AGUAAACA	286	UGUUUACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAAGGC	7686
1128	UUCUAAGU A AACAGUAU	287	AUACUGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUUAGAA	7687
1135	UAAACAGU A UGUGAACC	288	GGUUCACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGUUUA	7688
1145	GUGAACCU U UACCCCGU	289	ACGGGGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUCAC	7689
1146	UGAACCUU U ACCCCGUU	290	AACGGGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGUUCA	7690
1147	GAACCUUU A CCCCUGU	291	CAACGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGGUUC	7691
1154	UACCCCGU U GCUCGGCA	292	UGCCGAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGGGUA	7692
1158	CCGUUGCU C GGCAACGG	293	CCGUUGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAACGG	7693
1173	GGCCUGGU C UAUGCCAA	294	UUGGCAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCAGGCC	7694
1175	CCUGGUCU A UGCCAAGU	295	ACUUGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCAGG	7695
1186	CCAAGUGU U UGCUGACG	296	CGUCAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACUUGG	7696
1187	CAAGUGUU U GCUGACGC	297	GCGUCAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACACUUG	7697
1209	CCACUGGU U GGGGCUUG	298	CAAGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCAGUGG	7698
1216	UUGGGGCU U GGCCAUAG	299	CUAUGGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCCCAA	7699
1223	UUGGCCAU A GGCCAUCA	300	UGAUGGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGCCAA	7700
1230	UAGGCCAU C AGCGCAUG	301	CAUGCGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGCCUA	7701
1249	UGGAACCU U UGUGUCUC	302	GAGACACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUCCA	7702
1250	GGAACCUU U GUGUCUCC	303	GGAGACAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGUUCC	7703
1255	CUUUGUGU C UCCUCUGC	304	GCAGAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACAAAG	7704
1257	UUGUGUCU C CUCUGCCG	305	CGCAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACACAA	7705
1260	UGUCUCCU C UGCCGAUC	306	GAUCGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGACA	7706
1268	CUGCCGAU C CAUACCGC	307	GCGGUAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCGGCAG	7707
1272	CGAUCCAU A CCGCGGAA	308	UUCCGCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGAUCG	7708
1283	GCGGAACU C CUAGCCGC	309	GCGGCUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUCCGC	7709
1286	GAACUCCU A GCCGCUUG	310	CAAGCGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGUUC	7710
1293	UAGCCGCU U GUUUUGCU	311	AGCAAAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCGGCUA	7711
1296	CCGCUUGU U UUGCUCGC	312	GCGAGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAGCGG	7712
1297	CGCUUGUU U UGCUCGCA	313	UGCGAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAAGCG	7713
1298	GCUUUUUU U GCUCGCAG	314	CUCGAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACAAGC	7714
1302	GUUUUGCU C GCAGCAGG	315	CCUGCGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAAAAC	7715
1312	CAGCAGGU C UGGGGCAA	316	UUGCCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUGCUG	7716
1325	GCAAAACU C AUCGGGAC	317	GUCCCCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUUUGC	7717
1328	AAACUCAU C GGGACUGA	318	UCAGUCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAGUUU	7718
1341	CUGACAAU U CUGUCGUG	319	CACGACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGUCAG	7719
1342	UGACAAUU C UGUCGUGC	320	GCACGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGUCA	7720
1346	AAUUCUGU C GUGCUCUC	321	GAGAGCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGAAUU	7721
1352	GUCGUGCU C UCCCGCAA	322	UUGCGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCACGAC	7722
1354	CGUGCUCU C CCGCAAU	323	AUUUGCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGCACG	7723
1363	CCGCAAU A UACAUCAU	324	AUGAUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUGCGG	7724
1365	GCAAUAU A CAUCAUUU	325	AAAUGAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUUUGC	7725
1369	AUAUACAU C AUUCCAUC	326	AUGGAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUAUUA	7726
1372	UACAUCAU U UCCAUGGC	327	GCCAUGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUGUA	7727
1373	ACAUCAUU U CCAUGGCU	328	AGCCAUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGAUGU	7728
1374	CAUCAUUU C CAUGGUG	329	CAGCCAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUGAUG	7729
1385	UGGUGUCU A GGCUGUGC	330	GCACAGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGCCA	7730
1406	AACUGGAU C CUACGCGG	331	CCGCGUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCAGUU	7731
1409	UGGAUCCU A CGCGGGAC	332	GUCCCGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAUCCA	7732
1420	CGGGACGU C CUUUGUUU	333	AAACAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUCCCG	7733
1423	GACGUCCU U UGUUUACG	334	CGUAAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGACGUC	7734

1424	ACGUCCUU U GUUUACGU	335	ACGUA AAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGACGU	7735
1427	UCCUUUGU U UACGUCCC	336	GGGACGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAAGGA	7736
1428	CCUUUGUU U ACGUCCCG	337	CGGGACGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAAAGG	7737
1429	CUUUUGUU A CGUCCCGU	338	ACGGGACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACAAAG	7738
1433	GUUUACGU C CCGUCGGC	339	GCCGACGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUAAAC	7739
1438	CGUCCCGU C GGCGCUGA	340	UCAGCGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGGACG	7740
1449	CGCUGAAU C CCGCGGAC	341	GUCCCGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCAGCG	7741
1465	CGACCCCU C CCGGGGCC	342	GGCCCCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGUCG	7742
1477	GGGCCGCU U GGGGCUCU	343	AGAGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCGGCCC	7743
1484	UUGGGGCU C UACCGCCC	344	GGGCGGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCCCAA	7744
1486	GGGGCUCU A CCGCCCGC	345	GCGGGCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGCCCC	7745
1496	CGCCCGCU U UCCCGCCU	346	AGGCGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCGGGCG	7746
1497	GCCCGCUU C UCCGCCUA	347	UAGGCGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCGGGC	7747
1499	CCGCUUCU C CGCCUAUU	348	AAUAGGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGCGG	7748
1505	CUCCGCCU A UUGUACCG	349	CGGUACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCGGAG	7749
1507	CCGCCUAU U GUACCGAC	350	GUCGGUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGCGCG	7750
1510	CCUAUUGU A CCGACCGU	351	ACGGUCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAUAGG	7751
1519	CCGACCGU C CACGGGGC	352	GCCCCGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGUCGG	7752
1534	GCGCACCU C UC UUACG	353	CGUAAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUGCGC	7753
1536	GCACCUCU C UUUACGCG	354	CGCGUAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGGUGC	7754
1538	ACCUCUCU U UACGCGGA	355	UCCGCGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGAGGU	7755
1539	CCUCUCUU U ACGCGGAC	356	GUCCCGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAGAGG	7756
1540	CUCUCUUU A CGCGGACU	357	AGUCCGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAGAG	7757
1549	CGCGGACU C CCCGUCUG	358	CAGACGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCGCG	7758
1555	CUCCCCGU C UGUGCCUU	359	AAGGCACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGGGAG	7759
1563	CUGUGCCU U CUCAUCUG	360	CAGAUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCACAG	7760
1564	UGUGCCUU C UCAUCUGC	361	GCAGAUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGCACA	7761
1566	UGCCUUCU C AUCUGCCG	362	CGGCAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGGCA	7762
1569	CUUCUCAU C UGCCGGAC	363	GUCCGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAGAAG	7763
1588	UGUGCACU U CGCUUCAC	364	GUGAAGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGCACA	7764
1589	GUGCACUU C GCUUCACC	365	GGUGAAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUGCAC	7765
1593	ACUUCGCU U CACCUCUG	366	CAGAGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCGAAGU	7766
1594	CUUCGCUU C ACCUCUGC	367	GCAGAGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCGAAG	7767
1599	CUUCACCU C UGCACGUC	368	GACGUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUGAAG	7768
1607	CUGCACGU C GCAUGGAG	369	CUCCAUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUGCAG	7769
1651	CCCAAGGU C UUGCAUAA	370	UUAUGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUUGGG	7770
1653	CAAGGUCU U GCAUAAGA	371	UCUUAUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCUUG	7771
1658	UCUUGCAU A AGAGGACU	372	AGUCCUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCAAGA	7772
1667	AGAGGACU C UUGGACUU	373	AAGUCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCUCU	7773
1669	AGGACUCU U GGACUUUC	374	GAAAGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGUCCU	7774
1675	CUUGGACU U UCAGCAAU	375	AUUGCUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCCAAG	7775
1676	UUGGACUU U CAGCAAUG	376	CAUUGCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUCCAA	7776
1677	UGGACUUU C AGCAAUGU	377	ACAUUGC U CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGUCCA	7777
1686	AGCAAUGU C AACGACCG	378	CGGUCGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUUGCU	7778
1699	ACCGACCU U GAGGCAUA	379	UAUGCCUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUCGGU	7779
1707	UGAGGCAU A CUUCAAG	380	CUUUGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCCUCA	7780
1710	GGCAUACU U CAAAGACU	381	AGUCUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAUGCC	7781
1711	GCAUACUU C AAAGACUG	382	CAGUCUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUAUGC	7782
1725	CUGUGUGU U UAAUGAGU	383	ACUCAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACACAG	7783
1726	UGUGUGUU U AAUGAGUG	384	CACUCAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACACACA	7784
1727	GUGUGUUU A AUGAGUGG	385	CCACUCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACACAC	7785

1743	GGAGGAGU U GGGGGAGG	386	CCUCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCCUCC	7786
1756	GAGGAGGU U AGGUUAAA	387	UUUAACCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUCCUC	7787
1757	AGGAGGUU A GGUUAAAG	388	CUUUAACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCUCU	7788
1761	GGUUAGGU U AAAGGUCU	389	AGACCUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUAACC	7789
1762	GUUAGGUU A AAGGUCUU	390	AAGACCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCUAAC	7790
1768	UUAAAGGU C UUUGUACU	391	AGUACAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUUUAA	7791
1770	AAAGGUCU U UGUACUAG	392	CUAGUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCUUU	7792
1771	AAGGUCUU U GUACUAGG	393	CCUAGUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACCUU	7793
1774	GUCUUUGU A CUAGGAGG	394	CCUCCUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAAGAC	7794
1777	UUUGUACU A GGAGGCUG	395	CAGCCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUACAAA	7795
1787	GAGGCUGU A GGCAUAAA	396	UUUAGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGCCUC	7796
1793	GUAGGCAU A AAUUGGUG	397	CACCAAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUAUG	7797
1797	GCAUAAAU U GGUGUGUU	398	AACACACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUAUG	7798
1805	UGGUGUGU U CACCAGCA	399	UGCUGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACACCA	7799
1806	GGUGUGUU C ACCAGCAC	400	GUGCUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACACACC	7800
1824	AUGCAACU U UUUCACCU	401	AGGUGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUGCAU	7801
1825	UGCAACUU U UUCACCUC	402	GAGGUGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUUGCA	7802
1826	GCAACUUU U UCACCUCU	403	AGAGGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGUUGC	7803
1827	CAACUUUU U CACCUCUG	404	CAGAGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAGUUG	7804
1828	AACUUUUU C ACCUCUGC	405	GCAGAGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAAGUU	7805
1833	UUUCACCU C UGCCUAU	406	AUUAGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUGAAA	7806
1839	CUCUGCCU A AUCAUCUC	407	GAGAUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCAGAG	7807
1842	UGCCUAUU C AUCUCAUG	408	CAUGAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAGGCA	7808
1845	CUAAUCAU C UCAUGUUC	409	GAACAUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUUAG	7809
1847	AAUCAUCU C AUGUUCAU	410	AUGAACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUGAUU	7810
1852	UCUCAUGU U CAUGUCCU	411	AGGACAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUGAGA	7811
1853	CUCAUGUU C AUGUCCUA	412	UAGGACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAUAGG	7812
1858	GUUCAUGU C CUACUGUU	413	AACAGUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUGAAC	7813
1861	CAUGUCCU A CUGUCAA	414	UUGAACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGACAUG	7814
1866	CCUACUGU U CAAGCCUC	415	GAGGCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGUAGG	7815
1867	CUACUGUU C AAGCCUCC	416	GGAGGCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAGUAG	7816
1874	UCAAGCCU C CAAGCUGU	417	ACAGCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCUUGA	7817
1887	CUGUGCCU U GGGUGGCU	418	AGCCACCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCACAG	7818
1896	GGGUGGCU U UGGGGCAU	419	AUGCCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCACCC	7819
1897	GGUGGCUU U GGGGCAUG	420	CAUGCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCACC	7820
1911	AUGGACAU U GACCCGUA	421	UACGGGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCCAU	7821
1919	UGACCCGU A UAAAGAAU	422	AUUCUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGGGUCA	7822
1921	ACCCGUAU A AAGAAUUU	423	AAAUUCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACGGGU	7823
1928	UAAAGAAU U UGGAGCUU	424	AAGCUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCUUUA	7824
1929	AAAGAAUU U GGAGCUUC	425	GAAGCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUCUUU	7825
1936	UUGGAGCU U CUGUGGAG	426	CUCCACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCUCCAA	7826
1937	UGGAGCUU C UGUGGAGU	427	ACUCCACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCUCCA	7827
1946	UGUGGAGU U ACUCUCUU	428	AAGAGAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCCACA	7828
1947	GUGGAGUU A CUCUCUUU	429	AAAGAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACUCCAC	7829
1950	GAGUUACU C UCUUUUUU	430	AAAAAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAACUC	7830
1952	GUUACUCU C UUUUUUGC	431	GCAAAAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGUAA	7831
1954	UACUCUCU U UUUUGCCU	432	AGGCAAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGAGUA	7832
1955	ACUCUCUU U UUUGCCUU	433	AAGGCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAGAGU	7833
1956	CUCUCUUU U UUGCCUUC	434	GAAGGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAGAG	7834
1957	UCUCUUUU U UGCCUUCU	435	AGAAGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAGAGA	7835
1958	CUCUUUUU U GCCUUCUG	436	CAGAAGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAAGAG	7836

1963	UUUUGCCU U CUGACUUC	437	GAAGUCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCAAAA	7837
1964	UUUGCCUU C UGACUUCU	438	AGAAGUCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGCAAA	7838
1970	UUCUGACU U CUUUCUU	439	AAGGAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCAGAA	7839
1971	UCUGACUU C UUUCUU	440	GAAGGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUCAGA	7840
1973	UGACUUCU U UCCUUCUA	441	UAGAAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGUCA	7841
1974	GACUUCUU U CCUUCUAU	442	AUAGAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAAGUC	7842
1975	ACUUCUUU C CUUCUAU	443	AAUAGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAAGU	7843
1978	UCUUUCCU U CUAUUCGA	444	UCGAAUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAAAGA	7844
1979	CUUUCUU C UAUUCGAG	445	CUCGAAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGAAAG	7845
1981	UUCCUUCU A UUCGAGAU	446	AUCUCGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGGAA	7846
1983	CCUUCUAU U CGAGAUUC	447	AGAUCUCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGAAGG	7847
1984	CUUCUAU C GAGAUUC	448	GAGAUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAGAAG	7848
1990	UUCGAGAU C UCCUCGAC	449	GUCGAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUCGAA	7849
1992	CGAGAUUC C CUCGACAC	450	GUGUCGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUCUCG	7850
1995	GAUCUCCU C GACACCGC	451	GCGGUGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGAUUC	7851
2006	CACCGCCU C UGCUCUGU	452	ACAGAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCGGUG	7852
2011	CCUCUGCU C UGUUUCGG	453	CCGAUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGAGG	7853
2015	UGCUCUGU A UCGGGGGG	454	CCCCCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGAGCA	7854
2017	CUCUGUAU C GGGGGGCC	455	GGCCCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACAGAG	7855
2027	GGGGGCCU U AGAGUCUC	456	GAGACUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCCCC	7856
2028	GGGGCCUU A GAGUCUCC	457	GGAGACUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGCCCC	7857
2033	CUUAGAGU C UCCGGAAC	458	GUUCCGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCUAAG	7858
2035	UAGAGUCU C CGGAACAU	459	AUGUCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACUCUA	7859
2044	CGGAACAU U GUUCACCU	460	AGGUGAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCCG	7860
2047	AACAUUGU U CACCUCAC	461	GUGAGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAAUGUU	7861
2048	ACAUUGUU C ACCUCACC	462	GGUGAGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAUGU	7862
2053	GUUCACCU C ACCAUACG	463	CGUAUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUGAAC	7863
2059	CUCACCAU A CGGCACUC	464	GAGUGCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGUGAG	7864
2067	ACGGCACU C AGGCAAGC	465	GCUUGCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGCCGU	7865
2077	GGCAAGCU A UUCUGUGU	466	ACACAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCUUGCC	7866
2079	CAAGCUAU U CUGUGUUG	467	CAACAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGCUUG	7867
2080	AAGCUAU C UGUGUUGG	468	CCAACACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAGCUU	7868
2086	UUCUGUGU U GGGGUGAG	469	CUCACCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACAGAA	7869
2096	GGGUGAGU U GAUGAAUC	470	GAUUCauc CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCACCC	7870
2104	UGAUGAAU C UAGCCACC	471	GGUGGCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCAUCA	7871
2106	AUGAAUCU A GCCACCUG	472	CAGGUGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUUCAU	7872
2125	UGGGAAGU A AUUUGGAA	473	UUCCAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCCCA	7873
2128	GAAGAAU U UGGAAGAU	474	AUCUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUACUUC	7874
2129	AAGUAAU U GGAAGAU	475	GAUCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUACUUC	7875
2137	UGGAAGAU C CAGCAUCC	476	GGAUGCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUCCA	7876
2144	UCCAGCAU C CAGGGAU	477	AUCCCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCUGGA	7877
2153	CAGGGAU U AGUAGUCA	478	UGACUACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCCUG	7878
2154	AGGGAU A GUAGUCAG	479	CUGACUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUCCCU	7879
2157	GAAUAGU A GUCAGCUA	480	UAGCUGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUAAUUC	7880
2160	UUAGUAGU C AGCUAUGU	481	ACAUAGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUACUAA	7881
2165	AGUCAGCU A UGUCAACG	482	CGUUGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCUGACU	7882
2169	AGCUAUGU C AACGUUAA	483	UUAACGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUAGCU	7883
2175	GUCAACGU U AAUUGGG	484	CCCAUUAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUUGAC	7884
2176	UCAACGUU A AUAUGGGC	485	GCCCAUUAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACGUUGA	7885
2179	ACGUUAAU A UGGGCCUA	486	UAGGCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUACGU	7886
2187	AUGGGCCU A AAAUCAG	487	CUGAUUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCCAU	7887

2193	CUAAAAU C AGACAACU	488	AGUUGUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUUAG	7888
2202	AGACAACU A UUGUGGUU	489	AACCACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUGUCU	7889
2204	ACAACUUAU U GUGGUUUC	490	GAAACCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGUUGU	7890
2210	AUUGUGGU U UCACAUUU	491	AAAUGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCACAAU	7891
2211	UUGUGGUU U CACAUUUC	492	GAAAUGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCACAA	7892
2212	UGUGGUUU C ACAUUUCC	493	GGAAAUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACCACA	7893
2217	UUUCACAU U UCCUGUCU	494	AGACAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUGAAA	7894
2218	UUCACAUU U CCUGUCUU	495	AAGACAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGUGAA	7895
2219	UCACAUUU C CUGUCUUA	496	UAAGACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUGUGA	7896
2224	UUUCCUGU C UUACUUUU	497	AAAAGUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGGAAA	7897
2226	UCCUGUCU U ACUUUUUG	498	CCAAAAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACAGGA	7898
2227	CCUGUCUU A CUUUUGGG	499	CCCAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACAGG	7899
2230	GUCUUACU U UUGGGCGA	500	UCGCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAAGAC	7900
2231	UCUUACUU U UGGGCGAG	501	CUCGCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUAAGA	7901
2232	CUUACUUU U GGGCGAGA	502	UCUCGCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGUAAG	7902
2247	GAAACUGU U CUUGAAUA	503	UAUUCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGUUUC	7903
2248	AAACUGUU C UUGAAUAU	504	AUAUUCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAGUUU	7904
2250	ACUGUUCU U GAAUAUUU	505	AAAUUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAACAGU	7905
2255	UCUUGAAU A UUUGGUGU	506	ACACCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCAAGA	7906
2257	UUGAAUAU U UGGUGUCU	507	AGACACCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUUCAA	7907
2258	UGAAUAUU U GGUGUCUU	508	AAGACACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUUCU	7908
2264	UUUGGUGU C UUUUGGAG	509	CUCCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACACCAA	7909
2266	UGGUGUCU U UUGGAGUG	510	CACUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACACCA	7910
2267	GGUGUCUU U UGGAGUGU	511	ACACUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACACC	7911
2268	GUGUCUUU U GGAGUGUG	512	CACACUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGACAC	7912
2280	GUGUGGAU U CGCACUCC	513	GGAGUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCACAC	7913
2281	UGUGGAUU C GCACUCCU	514	AGGAGUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUCCACA	7914
2287	UUCGCACU C CUCCUGCA	515	UGCAGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGCGAA	7915
2290	GCACUCCU C CUGCAUAU	516	AUAUGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGUGC	7916
2297	UCCUGCAU A UAGACCAC	517	GUGGUCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCAGGA	7917
2299	CUGCAUAU A GACCACCA	518	UGGUGUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUGCAG	7918
2317	AUGCCCCU A UCUUAUCA	519	UGAUAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGCAU	7919
2319	GCCCCUUA C UUAUCAAC	520	GUUGAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGGGGC	7920
2321	CCCUAUCU U AUCAACAC	521	GUGUUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUAGGG	7921
2322	CCUAUCUU A UCAACACU	522	AGUGUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAUAGG	7922
2324	UAUCUUUA C AACACUUC	523	GAAGUGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAGAUU	7923
2331	UCAACACU U CCGGAAAC	524	GUUUCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGUUGA	7924
2332	CAACACUU C CGGAAACU	525	AGUUUCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUGUUG	7925
2341	CGGAAACU A CUGUUGUU	526	AACAACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUUCCG	7926
2346	ACUACUGU U GUUAGACG	527	CGUCUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGUAGU	7927
2349	ACUGUUGU U AGACGAAG	528	CUUCGUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAACAGU	7928
2350	CUGUUGUU A GACGAAGA	529	UCUUCGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAACAG	7929
2366	AGGCAGGU C CCCUAGAA	530	UUCUAGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUGCCU	7930
2371	GGUCCCCU A GAAGAAGA	531	UCUUCUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGACC	7931
2383	GAAGAACU C CCUCGCCU	532	AGGCGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUCUUC	7932
2387	AACUCCCU C GCCUCGCA	533	UGCAGGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGAGUU	7933
2392	CCUCGCCU C GCAGACGA	534	UCGUCUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCGAGG	7934
2405	ACGAAGGU C UCAAUCGC	535	GCGAUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUUCGU	7935
2407	GAAGGUCU C AAUCGCCG	536	CGGCGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCUUC	7936
2411	GUCUCAAU C GCCGCGUC	537	GACGCGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGAGAC	7937
2419	CGCCGCGU C GCAGAAGA	538	UCUUCUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGCGGCG	7938

2429	CAGAAGAU C UCAAUCUC	539	GAGAUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUUCUG	7939
2431	GAAGAUCU C AAUCUCGG	540	CCGAGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUCUUC	7940
2435	AUCUCAAU C UCGGGAU	541	AUUCCCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGAGAU	7941
2437	CUCAAUCU C GGGAAUCU	542	AGAUUCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUUGAG	7942
2444	UCGGGAU C UCAAUGU	543	AACAUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUCCCGA	7943
2446	GGGAUCU C AAUGUAG	544	CUAACAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUUCCC	7944
2452	CUCAAUGU U AGUAUUC	545	GGAAUACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUUGAG	7945
2453	UCAAUGUU A GUUUCCU	546	AGGAUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAUUGA	7946
2456	AUGUUAGU A UUCUUGG	547	CCAAGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUAAACU	7947
2458	GUUAGUAU U CCUUGGAC	548	GUCCAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACUAA	7948
2459	UUAGUAU C CUUGGACA	549	UGUCCAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUACUAA	7949
2462	GUUUCCU U GGACACAU	550	AUGUGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAUAC	7950
2471	GGACACAU A AGGUGGGA	551	UCCACCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUUGCC	7951
2484	GGGAAACU U UACGGGGC	552	GCCCCGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUUCCC	7952
2485	GGAAACUU U ACGGGGCU	553	AGCCCCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUUUCC	7953
2486	GAAACUUU A CGGGGCU	554	AAGCCCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGUUUC	7954
2494	ACGGGGCU U UAUUCUUC	555	GAAGAAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCCCCGU	7955
2495	CGGGGCUU U AUUCUUCU	556	AGAAGAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCCCCG	7956
2496	GGGGCUUU A UUCUUCUA	557	UAGAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCCCC	7957
2498	GGCUUUAU U CUUCUACG	558	CGUAGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAAGCC	7958
2499	GCUUUAU C UUCUACGG	559	CCGUAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAAAGC	7959
2501	UUUAUUCU U CUACGGUA	560	UACCGUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAUAAA	7960
2502	UUUAUUCU C UACGGUAC	561	GUACCGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAAUAA	7961
2504	AUUCUUCU A CGGUACCU	562	AGGUACCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGAAU	7962
2509	UCUACGGU A CCUUGCUU	563	AAGCAAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCGUAGA	7963
2513	CGGUACCU U GCUUAAU	564	AUUAAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUACCG	7964
2517	ACCUUGCU U UAAUCCUA	565	UAGGAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAAGGU	7965
2518	CCUUGCUU U AAUCCUAA	566	UUAGGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGCAAGG	7966
2519	CUUGCUUU A AUCCUAAA	567	UUUAGGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGCAAG	7967
2522	GCUUAAU C CUAAUUGG	568	CCAUUUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAAAGC	7968
2525	UUAUCCU A AAUGGCAA	569	UUGCCAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAUUA	7969
2537	GGCAAACU C CUUCUUU	570	AAAAGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUUGCC	7970
2540	AAACUCCU U CUUUUCCU	571	AGGAAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGUUU	7971
2541	AACUCCU C UUUUCCUG	572	CAGGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGAGUU	7972
2543	CUCCUUCU U UUCUGAC	573	GUCAGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAGGAG	7973
2544	UCCUUCU U UCCUGACA	574	UGUCAGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAAGGA	7974
2545	CCUUCUUU U CCUGACAU	575	AUGUCAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAAGG	7975
2546	CUUCUUUU C CUGACAUU	576	AAUGUCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAAGAAG	7976
2554	CCUGACAU U CAUUUGCA	577	UGCAAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCAGG	7977
2555	CUGACAUU C AUUUGCAG	578	CUGCAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGUCAG	7978
2558	ACAUUCAU U UGCAGGAG	579	CUCCUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAAUGU	7979
2559	CAUUCAU U GCAGGAGG	580	CCUCCUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGAAUG	7980
2572	GAGGACAU U GUUGAUAG	581	CUAUC AAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCCUC	7981
2575	GACAUUGU U GAUAGAUG	582	CAUCUAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUUGUC	7982
2579	UUGUUGAU A GAUGUAG	583	CUUACAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCAACAA	7983
2585	AUAGAUGU A AGCAAUU	584	AAAUUGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUCUAU	7984
2592	UAAGCAAU U UGUGGGGC	585	GCCCCACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGCUUA	7985
2593	AAGCAAUU U GUGGGGCC	586	GGCCCCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUGCUU	7986
2605	GGGCCCCU U ACAGUAAA	587	UUUACUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGCC	7987
2606	GGCCCCU A CAGUAAA	588	AUUUACUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGGGCC	7988
2611	CUUACAGU A AAUGAAA	589	UUUUCAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGUAAG	7989

2629	AGGAGACU U AAUUAAC	590	GUUAAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUCUCCU	7990
2630	GGAGACUU A AAUUAACU	591	AGUUAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGUCUCC	7991
2634	ACUUAUUU U AACUAUGC	592	GCAUAGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUUAGU	7992
2635	CUUAAUUU A ACUAUGCC	593	GGCAUAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUUUAAG	7993
2639	AAUUAACU A UGCCUGCU	594	AGCAGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUAUUU	7994
2648	UGCCUGCU A GGUUUUAU	595	AUAAAACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCAGGCA	7995
2652	UGCUAGGU U UUAUCCCA	596	UGGGAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUAGCA	7996
2653	GCUAGGUU U UAUCCCAA	597	UUGGGAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCUAGC	7997
2654	CUAGGUUU U AUCCCAAU	598	AUUGGGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAACCUAG	7998
2655	UAGGUUUU U UCCCAAUG	599	CAUUGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAACCUA	7999
2657	GGUUUUUAU C CCAAUGUU	600	AACAUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAAACC	8000
2665	CCCAAUGU U ACUAAUAU	601	UAUUUAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUUGGG	8001
2666	CCAAUGUU A CUAAUAU	602	AUAUUUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACAUUGG	8002
2669	AUGUUACU A AAUAUUUG	603	CAAAUAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAACAU	8003
2673	UACUAAAU A UUUGCCCU	604	AGGGCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUAGUA	8004
2675	CUAAUAU U UGCCCUUA	605	UAAGGGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUUUAG	8005
2676	UAAUAUUU U GCCCUUAG	606	CUAAGGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUUUA	8006
2682	UUUGCCCU U AGAUAAAG	607	CUUUUUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGCAAA	8007
2683	UUGCCCUU A GAUAAAGG	608	CCUUUAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGGGCAA	8008
2687	CCUUAGAU A AAGGGAUC	609	GAUCCCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUAAGG	8009
2695	AAAGGGAU C AAACCGUA	610	UACGGUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCCUUU	8010
2703	CAAACCGU A UUAUCCAG	611	CUGGAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUUUUG	8011
2705	AACCGUAU U AUCCAGAG	612	CUCUGGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUACGGUU	8012
2706	ACCGUAUU A UCCAGAGU	613	ACUCUGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUACGGU	8013
2708	CGUAUUUAU C CAGAGUAU	614	AUACUCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAUACG	8014
2715	UCCAGAGU A UGUAGUUA	615	UAACUACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCUGGA	8015
2719	GAGUAUGU A GUUAAUCA	616	UGAUUAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAUACUC	8016
2722	UAUGUAGU U AAUCAUUA	617	UAAUGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUACAU	8017
2723	AUGUAGUU A AUCAUJAC	618	GUAAUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACUACAU	8018
2726	UAGUUAUU C AUUACUUC	619	GAAGUAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAACUA	8019
2729	UUAACAUU A ACUCCAG	620	CUGGAAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUUAA	8020
2730	UAAUCAUU A CUUCCAGA	621	UCUGGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGAUUA	8021
2733	UCAUUAUU U CCAGACGC	622	GCGUCUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAAUGA	8022
2734	CAUUAUUU C CAGACGCG	623	CGCUGUCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAAUG	8023
2747	CGCGACAU U AUUUACAC	624	GUGUAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGUCGCG	8024
2748	GCGACAUU A UUUACACA	625	UGUGUAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGUCGC	8025
2750	GACAUUAU U UACACACU	626	AGUGUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAAUGUC	8026
2751	ACAUUAUU U ACACACUC	627	GAGUGUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUGU	8027
2752	CAUUAUUU A CACACUCU	628	AGAGUGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUUG	8028
2759	UACACACU C UUUGGAAG	629	CUUCCAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUGUGUA	8029
2761	CACACUCU U UGGAAGGC	630	GCCUCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAGUGUG	8030
2762	ACACUCUU U GGAAGGCG	631	CGCCUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAGUGU	8031
2776	GCGGGGAU C UUAUAUAA	632	UUAUAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCCCGC	8032
2778	GGGGAUCU U AUUAUAAA	633	UUUAUAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUCCCC	8033
2779	GGGAUCUU A UUAUAAAG	634	CUUUUAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAUCUU	8034
2781	GAUCUUUAU A UAAAAGAG	635	CUCUUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAGAUAU	8035
2783	UCUUUAUU A AAAGAGAG	636	CUCUCUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUAAGA	8036
2793	AAGAGAGU C CACACGUA	637	UACGUGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUCUCUU	8037
2801	CCACACGU A GCGCCUCA	638	UGAGGCGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACGUGUGG	8038
2808	UAGCGCCU C AUUUUGCG	639	CGCAAAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCGCUA	8039
2811	CGCCUCAU U UUGCGGGU	640	ACCCGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAGGCG	8040

2812	GCCUCAUU U UGCGGGUC	641	GACCCGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGAGGC	8041
2813	CCUCAUUU U GCGGGUCA	642	UGACCCGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAUGAGG	8042
2820	UUGCGGGU C ACCAUUU	643	AAUAUGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCCGCAA	8043
2826	GUCACCAU A UUCUUGGG	644	CCCAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGGUGAC	8044
2828	CACCAUUA U CUUGGGAA	645	UUCCCAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUAUGGUG	8045
2829	ACCAUAUU C UUGGGAAC	646	GUUCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUAUGGU	8046
2831	CAUAUUCU U GGAACAA	647	UUGUUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAUAUG	8047
2843	AACAAGAU C UACAGCAU	648	AUGCUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUUGUU	8048
2845	CAAGAUCU A CAGCAUGG	649	CCAUGCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUCUUG	8049
2859	UGGGAGGU U GGUCUCC	650	GGAAGACC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCUCCCA	8050
2863	AGGUUGGU C UUCCAAAC	651	GUUUGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCAACCU	8051
2865	GUUGGUCU U CCAAACCU	652	AGGUUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGACCAAC	8052
2866	UUGGUCUU C CAAACCUC	653	GAGGUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGACCAA	8053
2874	CCAAACCU C GAAAAGGC	654	GCCUUUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUUUGG	8054
2895	GGACAAU C UUCUGUC	655	GACAGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUGUCC	8055
2897	ACAAUCU U UCUGUCCC	656	GGGACAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAUUUGU	8056
2898	CAAUCUU U CUGUCCCC	657	GGGGACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAUIUG	8057
2899	AAAUUUU C UGUCCCCA	658	UGGGGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAAGAUUU	8058
2903	CUUUCUGU C CCCAUCC	659	GGAUUGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGAAAG	8059
2910	UCCCCAAU C CCCUGGGA	660	UCCCAGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGGGGA	8060
2920	CCUGGGAU U CUUCCCCG	661	CGGGGAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCCCAGG	8061
2921	CUGGGAUU C UUCCCCGA	662	UCGGGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUCCAG	8062
2923	GGGAUUCU U CCCCGAUC	663	GAUCGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGAAUCCC	8063
2924	GGAUUCUU C CCCGAUCA	664	UGAUCGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAGAAUCC	8064
2931	UCCCCGAU C AUCAGUUG	665	CAACUGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCGGGGA	8065
2934	CCGAUCAU C AGUUGGAC	666	GUCCAACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGAUCGG	8066
2938	UCAUCAGU U GGACCCUG	667	CAGGGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGAUGA	8067
2950	CCCUGCAU U CAAAGCCA	668	UGGCUUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCAGGG	8068
2951	CCUGCAUU C AAAGCCAA	669	UUGGCUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGCAGG	8069
2962	AGCCAACU C AGUAAAU	670	GAUUUACU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUUGGCU	8070
2966	AACUCAGU A AAUCCAGA	671	UCUGGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGAGUU	8071
2970	CAGUAAAU C CAGAUUGG	672	CCAAUCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUUACUG	8072
2976	AUCCAGAU U GGGACCUC	673	GAGGUCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUCUGGAU	8073
2984	UGGGACCU C AACCCGCA	674	UGCGGGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGUCCCA	8074
3037	GGGAGCAU U CGGGCCAG	675	CUGGCCCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUGCUCCC	8075
3038	GGAGCAUU C GGGCCAGG	676	CCUGGCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AAUGCUC	8076
3049	GCCAGGGU U CACCCUC	677	GAGGGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACCCUGGC	8077
3050	CCAGGGUU C ACCCCUCC	678	GGAGGGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AACCCUGG	8078
3057	UCACCCCU C CCCAUGGG	679	CCCAUGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGGUGA	8079
3073	GGGACUGU U GGGUGGA	680	UCCACCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACAGUCCC	8080
3087	GGAGCCCU C ACGUCAG	681	CUGAGCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGGCUCC	8081
3093	CUCACGCU C AGGGCCUA	682	UAGGCCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCGUGAG	8082
3101	CAGGGCCU A CUCACAAC	683	GUUGUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCCUG	8083
3104	GGCCUACU C ACAACUGU	684	ACAGUUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGUAGGCC	8084
3123	CAGCAGCU C CUCCUCCU	685	AGGAGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGCUGCUG	8085
3126	CAGCUCCU C CUCCUGCC	686	GGCAGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGCUG	8086
3129	CUCCUCCU C CUGCCUCC	687	GGAGGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGAGGAG	8087
3136	UCCUGCCU C CACCAAUC	688	GAUUGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCAGGA	8088
3144	CCACCAAU C GGCAGUCA	689	UGACUGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AUUGGUGG	8089
3151	UCGGCAGU C AGGAAGGC	690	GCCUCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ACUGCCGA	8090
3165	GGCAGCCU A CUCCUUA	691	UAAGGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA AGGCUGCC	8091

3168	AGCCUACU C CCUUAUCU	692	AGAUAAAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUAGGCU	8092
3172	UACUCCCU U AUCUCCAC	693	GUGGAGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGGGAGUA	8093
3173	ACUCCCUU A UCUCACC	694	GGUGGAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AAGGGAGU	8094
3175	UCCCUUUAU C UCCACCUC	695	GAGGUGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUAAGGGA	8095
3177	CCUUAUCU C CACCUCUA	696	UAGAGGUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGAUAAAGG	8096
3183	CUCCACCU C UAAGGGAC	697	GUCCCUUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGGUGGAG	8097
3185	CCACCUCU A AGGGACAC	698	GUGUCCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGAGGUGG	8098
3195	GGGACACU C AUCCUCAG	699	CUGAGGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGUGUCCC	8099
3198	ACACUCAU C CUCAGGCC	700	GGCCUGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA AUGAGUGU	8100
3201	CUCAUCCU C AGGCCAUG	701	CAUGGCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA AGGAUGAG	8101

Input Sequence = AF100308. Cut Site = UH/.

Stem Length = 8 . Core Sequence = CUGAUGAG GCCGUUAGGC CGAA

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

Underlined region can be any X sequence or linker, as described herein.

TABLE VI: HUMAN HBV INOZYME AND SUBSTRATE SEQUENCE

Pos	Substrate	Seq ID	Inozyme	Seq ID
9	AACUCCAC C ACUUUCCA	702	UGGAAAGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGAGUU	8102
10	ACUCCACC A CUUCCAC	703	GUGGAAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGGAGU	8103
12	UCCACCAC U UCCACCA	704	UGGUGGAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGUGGA	8104
16	CCACUUUC C ACCAAACU	705	AGUUUGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAGUGG	8105
17	CACUUUCC A CCAAACUC	706	GAGUUUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAAGUG	8106
19	CUUCCAC C AAACUCUU	707	AAGAGUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGAAAG	8107
20	UUUCCACC A AACUCUUC	708	GAAGAGUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGGAAA	8108
24	CACCAAAC U CUUCAAGA	709	UCUUGAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUGGUG	8109
26	CCAAACUC U UCAAGAUC	710	GAUCUUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUUUGG	8110
29	AACUCUUC A AGAUCCCA	711	UGGGAUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGAGUU	8111
35	UCAAGAUC C CAGAGUCA	712	UGACUCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUUCUGA	8112
36	CAAGAUC C AGAGUCAG	713	CUGACUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAUCUUG	8113
37	AAGAUC C A GAGUCAGG	714	CCUGACUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGAUCUU	8114
43	CCAGAGUC A GGGCCUG	715	CAGGGCCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACUCUGG	8115
48	GUCAGGGC C CUGUACUU	716	AAGUACAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCCUGAC	8116
49	UCAGGGCC C UGUACUUU	717	AAAGUACA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCCUGA	8117
50	CAGGGCCC U GUACUUUC	718	GAAAGUAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGCCCUG	8118
55	CCCUGUAC U UUCUGCU	719	AGCAGGAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUACAGGG	8119
59	GUACUUUC C UGUGGUG	720	CACCAGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAGUAC	8120
60	UACUUUCC U GCUGGUGG	721	CCACCAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAAGUA	8121
63	UUUCCUGC U GGUGGCUC	722	GAGCCACC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGAAA	8122
70	CUGGUGGC U CCAGUUA	723	UGAACUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCACCAG	8123
72	GGUGGCUC C AGUUCAGG	724	CCUGAACU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGCCACC	8124
73	GUGGCUC C A GUUCAGGA	725	UCCUGAAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGCCAC	8125
78	UCCAGUUC A GGAACAGU	726	ACUGUUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAUCGGA	8126
84	UCAGGAAC A GUGAGCCC	727	GGGUCAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUCACUG	8127
91	CAGUGAGC C CUGCUCAG	728	CUGAGCAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUCACUG	8128
92	AGUGAGCC C UGCUCAGA	729	UCUGAGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCUCACU	8129
93	GUGAGCCC U GCUCAGAA	730	UUCUGAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGCUCAC	8130
96	AGCCUGC U CAGAAUAC	731	GUAUUCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGGCU	8131
98	CCCUGCUC A GAAUACUG	732	CAGUAUUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGCAGGG	8132
105	CAGAAUAC U GUCUCUGC	733	GCAGAGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUAAUUCUG	8133
109	AUACUGUC U CUGCCAUA	734	UAUGGCAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACAGUUA	8134
111	ACUGUCUC U GCCAUUAC	735	GAUAUGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGACAGU	8135
114	GUCUCUGC C AUAUCGUC	736	GACGAUUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGAGAC	8136
115	UCUCUGCC A UAUCGUCA	737	UGACGAUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCAGAGA	8137
123	AUAUCGUC A AUCUUAUC	738	GAUAAGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACGAUUA	8138
127	CGUCAUUC U UAUCGAAG	739	CUUCGAUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUUGACG	8139
138	UCGAAGAC U GGGGACCC	740	GGGUCCCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCUCCGA	8140
145	CUGGGGAC C CUGUACCG	741	CGGUACAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCCCAG	8141
146	UGGGGACC C UGUACCGA	742	UCGGUACA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUCCCCA	8142
147	GGGGACCC U GUACCGAA	743	UUCGGUAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGUCCCC	8143
152	CCUGUAC C GAACAUGG	744	CCAUGUUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUACAGGG	8144
157	UACCGAAC A UGGAGAAC	745	GUUCUCCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCGGUA	8145
166	UGGAGAAC A UCGCAUCA	746	UGAUGCGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCUCCA	8146
171	AACAUCGC A UCAGGACU	747	AGUCCUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGAUGUU	8147

174	AUCGCAUC A GGACUCCU	748	AGGAGUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUGCGAU	8148
179	AUCAGGAC U CCUAGGAC	749	GUCCUAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCUGAU	8149
181	CAGGACUC C UAGGACCC	750	GGGUCCUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUCCUG	8150
182	AGGACUCC U AGGACCCC	751	GGGGUCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGUCCU	8151
188	CCUAGGAC C CCUGCUCG	752	CGAGCAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCUAGG	8152
189	CUAGGACC C CUGCUCGU	753	ACGAGCAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUCCUAG	8153
190	UAGGACCC C UGCUCGUG	754	CACGAGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGUCCUA	8154
191	AGGACCCC U GCUCGUGU	755	ACACGAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGGUCCU	8155
194	ACCCUGC U CGUGUUAC	756	GUAACACG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGGGU	8156
203	CGUGUUAC A GCGGGGU	757	ACCCCGCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUAACACG	8157
217	GGUUUUUC U UGUUGACA	758	UGUCAACA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAAACC	8158
225	UUGUUGAC A AAAAUCCU	759	AGGAUUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCAACAA	8159
232	CAAAAAUC C UCACAAUA	760	UAUUGUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUUUUUG	8160
233	AAAAAUCC U CACAAUAC	761	GUAAUUGUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAUUUUU	8161
235	AAAUCCUC A CAUAACCA	762	UGGUUUUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGAUUU	8162
237	AUCCUCAC A AUACCACA	763	UGUGGUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGAGGAU	8163
242	CACAAUAC C ACAGAGUC	764	GACUCUGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUAUUGUG	8164
243	ACAAUACC A CAGAGUCU	765	AGACUCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUAUUGU	8165
245	AAUACCAC A GAGUCUAG	766	CUAGACUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGUUUU	8166
251	ACAGAGUC U AGACUCGU	767	ACGAGUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACUCUGU	8167
256	GUCUAGAC U CGUGUGUG	768	CCACCACG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCUAGAC	8168
267	UGGUGGAC U UCUCUCAA	769	UUGAGAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCACCA	8169
270	UGGACUUC U CUCAAUUU	770	AAAUUGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGUCCA	8170
272	GACUUCUC U CAAUUUUC	771	GAAAAUUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGAAGUC	8171
274	CUUCUCUC A AUUUUCUA	772	UAGAAAAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGAGAAG	8172
281	CAAUUUUC U AGGGGGAA	773	UUCCCCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAAUUG	8173
291	GGGGGAAC A CCCGUGUG	774	CACACGGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCCCCC	8174
293	GGGAACAC C CGUGUGUC	775	GACACACG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGUCCCC	8175
294	GGAACACC C GUGUGUCU	776	AGACACAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGUCCC	8176
302	CGUGUGUC U UGGCCAAA	777	UUUGGCCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACACACG	8177
307	GUCUUGGC C AAAAUUCG	778	CGAAUUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCAAGAC	8178
308	UCUUGGCC A AAUUCGC	779	GCGAAUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCCAAGA	8179
317	AAAUUCGC A GUCCAAA	780	UUUGGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGAAUUU	8180
321	UCGCAGUC C CAAAUUC	781	GAGAUUUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACUGCGA	8181
322	CGCAGUCC C AAUUCUC	782	GGGAUUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGACUGCG	8182
323	GCAGUCCC A AAUCUCCA	783	UGGAGAUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAUUGCG	8183
328	CCCAAUUC U CCAGUCAC	784	GUGACUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUUUGGG	8184
330	CAAAUCUC C AGUCACUC	785	GAGUGACU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGAUUUG	8185
331	AAAUUCUC A GUCACUCA	786	UGAGUGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGAUUU	8186
335	CUCCAGUC A CUCACCAA	787	UUGGUGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACUGGAG	8187
337	CCAGUCAC U CACCAACC	788	GGUUGGUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGACUGG	8188
339	AGUCACUC A CCAACCUG	789	CAGGUUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUGACU	8189
341	UCACUCAC C AACCGUU	790	AACAGGUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGAGUGA	8190
342	CACUCACC A ACCUGUUG	791	CAACAGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGAGUG	8191
345	UCACCAAC C UGUUGUCC	792	GGACAACA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGGUGA	8192
346	CACCAACC U GUUGUCCU	793	AGGACAAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUUGGUG	8193
353	CUGUUGUC C UCCAAUUU	794	AAAUUGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACAACAG	8194
354	UGUUGUCC U CCAAUUUG	795	CAAAUUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGACAACA	8195
356	UUGUCCUC C AAUUGUC	796	GACAAAUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGACAA	8196
357	UGUCCUCC A AUUUGUCC	797	GGACAAAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGGACA	8197
365	AAUUGUC C UGUUAUC	798	GAUAACCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACAAAUU	8198

366	AUUUGUCC U GGUUAUCG	799	CGAUAACC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGACAAAU	8199
376	GUUAUCGC U GGAUGUGU	800	ACACAUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGAUAAC	8200
386	GAUGUGUC U GCGGCGUU	801	AACGCCGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACACAUC	8201
400	GUUUUAUC A UCUCUCC	802	GAGGAAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUAAAAC	8202
403	UUAUCAUC U UCCUCUGC	803	GCAGAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUGAUAA	8203
406	UCAUCUUC C UCUGCAUC	804	GAUGCAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGAUGA	8204
407	CAUCUUC C UCUGCAUC	805	GGAUGCAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAGAUG	8205
409	UCUCCUC U GCAUCCUG	806	CAGGAUGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGAAGA	8206
412	UCCUCUGC A UCCUCUG	807	CAGCAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGAGGA	8207
415	UCUGCAUC C UGCGCUA	808	UAGCAGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUGCAGA	8208
416	CUGCAUCC U GCUAUGCC	809	AUAGCAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAUGCAG	8209
419	CAUCCUGC U GCUAUGCC	810	GGCAUAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGAUG	8210
422	CCUGCUGC U AUGCCUCA	811	UGAGGCAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGCAGG	8211
427	UGCUAUGC C UCAUCUUC	812	GAAGAUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAUAGCA	8212
428	GCUAUGCC U CAUCUUCU	813	AGAAGAUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCAUAGC	8213
430	UAUGCCUC A UCUCUUG	814	CAAGAAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGCAUA	8214
433	GCCUCAUC U UCUCUUG	815	CAACAAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUGAGGC	8215
436	UCAUCUUC U UGUUGGUU	816	AACCAACA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGAUGA	8216
446	GUUGGUUC U UCUGGACU	817	AGUCCAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAACCAAC	8217
449	GGUUCUUC U GGACUAUC	818	GAUAGUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGAACC	8218
454	UUCUGGAC U AUCAAGGU	819	ACCUUGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCAGAA	8219
458	GGACUAUC A AGGUAUGU	820	ACAUACCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUAGUCC	8220
470	UAUGUUGC C CGUUGUC	821	GACAAACG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAACAUA	8221
471	AUGUUGCC C GUUUGUCC	822	GGACAAAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCAACAU	8222
479	CGUUGUC C UCUAUUC	823	GAAUUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACAAACG	8223
480	GUUUGUCC U CUAAUUC	824	GGAUUAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGACAAAC	8224
482	UUGUCCUC U AAUCCAG	825	CUGGAAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGACAA	8225
488	UCUAUUC C AGGAUCAU	826	AUGAUCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAUUGA	8226
489	CUAAUUC A GGAUCAUC	827	GAUGAUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAUUG	8227
495	CCAGGAUC A UCAACAAC	828	GUUGUUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUCCUGG	8228
498	GGAUCAUC A ACAACCAG	829	CUGGUUGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUGAUCC	8229
501	UCAUCAAC A ACCAGCAC	830	GUGCUGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGAUGA	8230
504	UCAACAAC C AGCACCGG	831	CCGUGUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGUUGA	8231
505	CAACAACC A GCACCGGA	832	UCCGGUGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGUUG	8232
508	CAACCAGC A CCGACCA	833	UGGUCCGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUGGUUG	8233
510	ACCAGCAC C GGACCAUG	834	CAUGGUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGCUGGU	8234
515	CACCGGAC C AUGCAAAA	835	UUUGCAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCGGUG	8235
516	ACCGGACC A UGCAAAAC	836	GUUUGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUCCGGU	8236
520	GACCAUGC A AAACCUGC	837	GCAGGUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAUGGUC	8237
525	UGCAAAAC C UGCACAAC	838	GUUGUGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUUGCA	8238
526	GCAAAACC U GCACAACU	839	AGUUGUGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUUUGC	8239
529	AAACCUGC A CAACUCCU	840	AGGAGUUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGUUU	8240
531	ACCUGCAC A ACUCCUGC	841	GCAGGAGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGCAGGU	8241
534	UGCACAAC U CCUGCUC	842	UGAGCAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGUGCA	8242
536	CACAACUC C UGCUCAAG	843	CUUGAGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUUGUG	8243
537	ACAACUCC U GCUCAAGG	844	CCUUGAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGUUGU	8244
540	ACUCCUGC U CAAGGAAC	845	GUUCCUUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGAGU	8245
542	UCCUGCUC A AGGAACCU	846	AGGUUCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGCAGGA	8246
549	CAAGGAAC C UCUAUGUU	847	AACAUAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCCUUG	8247
550	AAGGAACC U CUAUGUUU	848	AAACAUAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUCCUUC	8248
552	GGAACCUC U AUGUUUCC	849	GGAACAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGUUCC	8249

560	UAUGUUUC C CUCAUGUU	850	AACAUGAG CUGAUGAG	GCCGUUAGGC	CGAA	IAAACAU	8250
561	AUGUUUCC C UCAUGUUG	851	CAACAUGA CUGAUGAG	GCCGUUAGGC	CGAA	IGAAACAU	8251
562	UGUUUCCC U CAUGUUGC	852	GCAACAUG CUGAUGAG	GCCGUUAGGC	CGAA	IGGAAACA	8252
564	UUUCCCUC A UGUUGCUG	853	CAGCAACA CUGAUGAG	GCCGUUAGGC	CGAA	IAGGGAAA	8253
571	CAUGUUGC U GUACAAA	854	UUUUGUAC CUGAUGAG	GCCGUUAGGC	CGAA	ICAACAUG	8254
576	UGCUGUAC A AAACCUAC	855	GUAGGUUU CUGAUGAG	GCCGUUAGGC	CGAA	IUACAGCA	8255
581	UACAAAAC C UACGGACG	856	CGUCCGUA CUGAUGAG	GCCGUUAGGC	CGAA	IUUUUGUA	8256
582	ACAAAACC U ACGGACGG	857	CCGUCCGU CUGAUGAG	GCCGUUAGGC	CGAA	IGUUUUGU	8257
595	ACGGAAAC U GCACCUGU	858	ACAGGUGC CUGAUGAG	GCCGUUAGGC	CGAA	IUUUCCGU	8258
598	GAAACUGC A CCUGUAUU	859	AAUACAGG CUGAUGAG	GCCGUUAGGC	CGAA	ICAGUUUC	8259
600	AACUGCAC C UGUAUUCC	860	GGAUAACA CUGAUGAG	GCCGUUAGGC	CGAA	IUGCAGUU	8260
601	ACUGCAC C UGUAUUCC	861	GGGAUAUAC CUGAUGAG	GCCGUUAGGC	CGAA	IGUGCAGU	8261
608	CUGUAUUC C CAUCCCAU	862	AUGGGAUG CUGAUGAG	GCCGUUAGGC	CGAA	IAAUACAG	8262
609	UGUAUUC C AUCCCAUC	863	GAUGGGAU CUGAUGAG	GCCGUUAGGC	CGAA	IGAAUACA	8263
610	GUUAUCCC A UCCCAUCA	864	UGAUGGGA CUGAUGAG	GCCGUUAGGC	CGAA	IGGAAUAC	8264
613	UUCCCAUC C CAUCAUCU	865	AGAUGAUG CUGAUGAG	GCCGUUAGGC	CGAA	IAUGGGAA	8265
614	UCCCAUCC C AUCAUCU	866	AAGAUGAU CUGAUGAG	GCCGUUAGGC	CGAA	IGAUGGGA	8266
615	CCCAUCCC A UCAUCUUG	867	CAAGAUGA CUGAUGAG	GCCGUUAGGC	CGAA	IGAUGGGG	8267
618	AUCCCAUC A UCUGGGC	868	GCCCAAGA CUGAUGAG	GCCGUUAGGC	CGAA	IAUGGGAU	8268
621	CCAUCUUC U UGGGCUUU	869	AAAGCCCA CUGAUGAG	GCCGUUAGGC	CGAA	IAUGAUGG	8269
627	UCUUGGGC U UUCGCAA	870	UUUGCGAA CUGAUGAG	GCCGUUAGGC	CGAA	ICCCAAGA	8270
633	GCUUUCGC A AAUACCU	871	AGGUUAUU CUGAUGAG	GCCGUUAGGC	CGAA	ICGAAAGC	8271
640	CAAAUAC C UAUGGGAG	872	CUCCCAUA CUGAUGAG	GCCGUUAGGC	CGAA	IUAUUUUG	8272
641	AAAUUACC U AUGGGAGU	873	ACUCCCAU CUGAUGAG	GCCGUUAGGC	CGAA	IGUAUUUU	8273
654	GAGUGGGC C UCAGUCCG	874	CGGACUGA CUGAUGAG	GCCGUUAGGC	CGAA	ICCCACUC	8274
655	AGUGGGCC U CAGUCCGU	875	ACGGACUG CUGAUGAG	GCCGUUAGGC	CGAA	IGCCACU	8275
657	UGGGCCUC A GUCCGUUU	876	AAACGGAC CUGAUGAG	GCCGUUAGGC	CGAA	IAGGCCCA	8276
661	CCUCAGUC C GUUUCUCU	877	AGAGAAAC CUGAUGAG	GCCGUUAGGC	CGAA	IACUGAGG	8277
667	UCCGUUUC U CUUGGCUC	878	GAGCCAAG CUGAUGAG	GCCGUUAGGC	CGAA	IAAACGGA	8278
669	CGUUUCUC U UGGCUCAG	879	CUGAGCCA CUGAUGAG	GCCGUUAGGC	CGAA	IAGAAACG	8279
674	CUCUUGGC A CAGUUUAC	880	GUAAACUG CUGAUGAG	GCCGUUAGGC	CGAA	ICCAAGAG	8280
676	CUUGGCUC A GUUUAUA	881	UAGUAAAC CUGAUGAG	GCCGUUAGGC	CGAA	IAGCCAAG	8281
683	CAGUUUAC U AGUGCCAU	882	AUGGCACU CUGAUGAG	GCCGUUAGGC	CGAA	IUAAACUG	8282
689	ACUAGUGC C AUUUGUUC	883	GAACAAAU CUGAUGAG	GCCGUUAGGC	CGAA	ICACUAGU	8283
690	CUAGUGCC A UUUGUUA	884	UGAACAAA CUGAUGAG	GCCGUUAGGC	CGAA	IGCACUAG	8284
698	AUUUGUUC A GUGGUUCG	885	CGAACCAC CUGAUGAG	GCCGUUAGGC	CGAA	IAACAAAU	8285
713	CGUAGGGC U UUCCCCCA	886	UGGGGGAA CUGAUGAG	GCCGUUAGGC	CGAA	ICCCUACG	8286
717	GGGCUUUC C CCCACUGU	887	ACAGUGGG CUGAUGAG	GCCGUUAGGC	CGAA	IAAAGCCC	8287
718	GGCUUUC C CCACUGUC	888	GACAGUGG CUGAUGAG	GCCGUUAGGC	CGAA	IGAAAGCC	8288
719	GCUUUCCC C CACUGUCU	889	AGACAGUG CUGAUGAG	GCCGUUAGGC	CGAA	IGGAAAGC	8289
720	CUUUCCCC C ACUGUCUG	890	CAGACAGU CUGAUGAG	GCCGUUAGGC	CGAA	IGGGAAAG	8290
721	UUUUCCCC A CUGUCUGG	891	CCAGACAG CUGAUGAG	GCCGUUAGGC	CGAA	IGGGGAAA	8291
723	UCCCCCAC U GUCUGGCU	892	AGCCAGAC CUGAUGAG	GCCGUUAGGC	CGAA	IUGGGGGA	8292
727	CCACUGUC U GGCUUUCA	893	UGAAAGCC CUGAUGAG	GCCGUUAGGC	CGAA	IACAGUGG	8293
731	UGUCUGGC U UUCAGUUA	894	UAACUGAA CUGAUGAG	GCCGUUAGGC	CGAA	ICCAGACA	8294
735	UGGCUUUC A GUUAUAUG	895	CAUAUAAC CUGAUGAG	GCCGUUAGGC	CGAA	IAAAGCCA	8295
764	UUGGGGGC C AAGUCUGU	896	ACAGACUU CUGAUGAG	GCCGUUAGGC	CGAA	ICCCCAA	8296
765	UGGGGGCC A AGUCUGUA	897	UACAGACU CUGAUGAG	GCCGUUAGGC	CGAA	IGCCCCCA	8297
770	GCCAAGUC U GUACAACA	898	UGUUGUAC CUGAUGAG	GCCGUUAGGC	CGAA	IACUUGGC	8298
775	GUCUGUAC A ACAUCUUG	899	CAAGAUGU CUGAUGAG	GCCGUUAGGC	CGAA	IUACAGAC	8299
778	UGUACAAC A UCUUGAGU	900	ACUCAAGA CUGAUGAG	GCCGUUAGGC	CGAA	IUUGUACA	8300

781	ACAACAUC U UGAGUCCC	901	GGGACUCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUGUUGU	8301
788	CUUGAGUC C CUUUAUGC	902	GCAUAAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACUCAAG	8302
789	UUGAGUCC C UUUUAUGCC	903	GGCAUAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGACUCA	8303
790	UGAGUCCC U UUAUGCCG	904	CGGCAUAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGACUCA	8304
797	CUUUAUGC C GCUGUUAC	905	GUAACAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAUAAAG	8305
800	UAUGCCGC U GUUACCAA	906	UUGGUAAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGCAUA	8306
806	GCUGUUAC C AAUUUUCU	907	AGAAAAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUAACAGC	8307
807	CUGUUACC A AUUUUCU	908	AAGAAAAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUAACAG	8308
814	CAAUUUUC U UUUGUCU	909	AAGACAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAAUUG	8309
821	CUUUUGUC U UUGGGUAA	910	AUACCCAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACAAAAG	8310
832	GGGUAAUC A UUAAAACC	911	GGUUUAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUAACCC	8311
840	AUUUAAAC C UCACAAA	912	UUUGUGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUAAA	8312
841	UUUAAACC C UCACAAA	913	UUUUGUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUUUAAA	8313
842	UUAACCC U CACAAAAC	914	GUUUUGUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGUUUAA	8314
844	AAACCCUC A CAAAACAA	915	UUGUUUUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGGUUU	8315
846	ACCCUCAC A AAACAAA	916	UUUUGUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGGUU	8316
851	CACAAAAC A AAAAGAU	917	CAUCUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUUGUG	8317
869	GGAUUUUC C CUUAACU	918	AAGUUAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAUAUCC	8318
870	GAUAUUCC C UUAACUUC	919	GAAGUUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAUAUC	8319
871	AUAUCCC U UAACUUC	920	UGAAGUUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAUAU	8320
876	CCCUAAC U UCAUGGGA	921	UCCCAUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUAAGGG	8321
879	UUAACUUC A UGGGAUUA	922	AUAUCCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGUUA	8322
906	GUUGGGGC A CAUUGCCA	923	UGGCAAUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCCCAAC	8323
908	UGGGGCAC A UUGCCACA	924	UGUGGCAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGCCCA	8324
913	CACAUUGC C ACAGGAAC	925	GUUCCUGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAUGUG	8325
914	ACAUUGCC A CAGGAACA	926	UGUCCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCAUGU	8326
916	AUUGCCAC A GGAACUA	927	UAUGUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGCAU	8327
922	ACAGGAAC A UAUUGUAC	928	GUACAAUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCCUGU	8328
931	UAUUGUAC A AAAAUCA	929	UGAUUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUACAAUA	8329
939	AAAAAUUC A AAUUGUGU	930	ACACAUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUUUUU	8330
958	UAGGAAAC U UCCUGUAA	931	UUACAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUCCUA	8331
961	GAAACUUC C UGUAAACA	932	UGUUUACA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGUUUC	8332
962	AAACUUC C UGUAAACAG	933	CUGUUUAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAGUU	8333
969	CUGUAAAC A GGCCUAU	934	AAUAGGCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUACAG	8334
973	AAACAGGC C UAUUGAU	935	AAUCAUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCUGUU	8335
974	AACAGGCC U AUUGAUUG	936	CAAUCAAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCUGUU	8336
994	AGUAUGUC A ACGAAUUG	937	CAAUUCGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACAUACU	8337
1009	UGUGGGUC U UUUGGGU	938	ACCCCAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACCACA	8338
1022	GGGUUUGC C GCCCUUU	939	AAAGGGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAAACCC	8339
1025	UUUGCCGC C CCUUCAC	940	GUGAAAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGCAAA	8340
1026	UUGCCGCC C CUUUCACG	941	CGUGAAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGCAA	8341
1027	UGCCGCC C UUUCACGC	942	GCGUGAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGCGCA	8342
1028	GCCGCC C UUUCACGCA	943	UGCGUGAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGCGGC	8343
1032	CCCUUUC A CGCAAUGU	944	ACAUUGCG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAGGG	8344
1036	UUUCACGC A AUGUGAU	945	AUCCACAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGUGAA	8345
1049	GGAUUUUC U GCUUAAU	946	AUUAAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAUAUCC	8346
1052	UAUUCUGC U UUAUUGCC	947	GGCAUUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGAAUA	8347
1060	UUUAAUGC C UUAUAUG	948	CAUAUAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAUAAA	8348
1061	UUAUUGCC U UUAUAUGC	949	GCAUAUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCAUUA	8349
1070	UUAUAUGC A UGCAUACA	950	UGUAUGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAUAUA	8350
1074	AUGCAUGC A UACAAGCA	951	UGCUGUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAUGCAU	8351

1078	AUGCAUAC A AGCAAAAC	952	GUUUUGCU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUAUGCAU	8352
1082	AUACAAGC A AAACAGGC	953	GCCUGUUU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICUUGUAU	8353
1087	AGCAAAAC A GGCUUUUA	954	UAAAAGCC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUUUGCU	8354
1091	AAACAGGC U UUUACUUU	955	AAAGUAAA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICCUGUUU	8355
1097	GCUUUUAC U UUCUCGCC	956	GGCGAGAA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUAAAAGC	8356
1101	UUACUUUC U CGCCAACU	957	AGUUGGCG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAAAGUAA	8357
1105	UUUCUCGC C AACUUACA	958	UGUAAGUU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICGAGAAA	8358
1106	UUCUCGCC A ACUUACAA	959	UUGUAAGU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICGAGAA	8359
1109	UCGCCAAC U UACAAGGC	960	GCCUUGUA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUGGCGA	8360
1113	CAACUUAC A AGGCCUUU	961	AAAGGCCU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUAAGUUG	8361
1118	UACAAGGC C UUCUAAG	962	CUUAGAAA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICCUUGUA	8362
1119	ACAAGGCC U UUCUAAGU	963	ACUUAGAA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGCCUUGU	8363
1123	GGCCUUUC U AAGUAAAC	964	GUUUACUU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAAAGGCC	8364
1132	AAGUAAAC A GUAUGUGA	965	UCACAUAC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUACUU	8365
1143	AUGUGAAC C UUUACCCC	966	GGGGUAAA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUCACAU	8366
1144	UGUGAAC C UUUACCCC	967	CGGGGUAA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGUUCACA	8367
1149	ACCUUUAC C CCGUUGCU	968	AGCAACGG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUAAAGGU	8368
1150	CCUUUACC C CGUUGCUC	969	GAGCAACG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGUAAAGG	8369
1151	CUUUACCC C GUUGCUCG	970	CGAGCAAC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGGUAAAG	8370
1157	CCCGUUGC U CGGCAACG	971	CGUUGCCG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICAACGGG	8371
1162	UGCUCGGC A ACGGCCUG	972	CAGGCCGU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICCGAGCA	8372
1168	GCAACGGC C UGGUCUAU	973	AUAGACCA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICCGUUGC	8373
1169	CAACGGCC U GGUUAUG	974	CAUAGACC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGCCGUUG	8374
1174	GCCUGGUC U AUGCCAAG	975	CUUGGCAU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IACCAGGC	8375
1179	GUCUAUGC C AAGUGUUU	976	AAACACUU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICAUAGAC	8376
1180	UCUAUGCC A AGUGUUUG	977	CAAACACU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGCAUAGA	8377
1190	GUGUUUGC U GACGCAAC	978	GUUGCGUC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICAAACAC	8378
1196	GCUGACGC A ACCCCAC	979	GUGGGGGU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICGUCAGC	8379
1199	GACGCAAC C CCCACUGG	980	CCAGUGGG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUGCGUC	8380
1200	ACGCAACC C CCACUGGU	981	ACCAGUGG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGUUGCGU	8381
1201	CGCAACCC C CACUGGUU	982	AACCAGUG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGGUUGCG	8382
1202	GCAACCCC C ACUGGUUG	983	CAACCAGU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGGGUUGC	8383
1203	CAACCCCC A CUGGUUGG	984	CCAACCAG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGGGGUUG	8384
1205	ACCCCCAC U GGUUGGGG	985	CCCCAACC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUGGGGUU	8385
1215	GUUGGGGC U UGGCCAU	986	UAUGGCCA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICCCAAC	8386
1220	GGCUUGGC C AUAGGCCA	987	UGGCCUAU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICCAAGCC	8387
1221	GCUUGGCC A UAGGCCAU	988	AUGGCCUA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGCCAAGC	8388
1227	CCAUAGGC C AUCAGCGC	989	GCGCUGAU CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICCUAUGG	8389
1228	CAUAGGCC A UCAGCGCA	990	UGCUCUGA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGCCUUG	8390
1231	AGGCCAUC A GCGAUGC	991	GCAUGC GC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAUGGCCU	8391
1236	AUCAGCGC A UGCGUGGA	992	UCCACGCA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICGCUGAU	8392
1247	CGUGGAAC C UUGUGUC	993	GACACAAA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUUCCACG	8393
1248	GUGGAACC U UUGUGUCU	994	AGACACAA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGUUCAC	8394
1256	UUUGUGUC U CCUCUGCC	995	GGCAGAGG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IACACAAA	8395
1258	UGUGUCUC C UCUGCCGA	996	UCGGCAGA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAGACACA	8396
1259	GUGUCUCC U CUGCCGAU	997	AUCGGCAG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGAGACAC	8397
1261	GUCUCCUC U GCCGAUCC	998	GGAUCGGC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAGGAGAC	8398
1264	UCCUCUGC C GAUCCAUA	999	UAUGGAUC CUGAUGAG	<u>GCCGUUAGGC</u> CGAA ICAGAGGA	8399
1269	UGCCGAUC C AUACGCG	1000	CGCGGUUA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IAUCCGCA	8400
1270	GCCGAUCC A UACCGCG	1001	CCGCGGUA CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IGAUCGGC	8401
1274	AUCCAUA C GCGGAACU	1002	AGUCCGCG CUGAUGAG	<u>GCCGUUAGGC</u> CGAA IUAUGGAU	8402

1282	CGCGGAAC U CCUAGCCG	1003	CGGCUAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCCGCG	8403
1284	CGGAACUC C UAGCCGCU	1004	AGCGGCUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUCCG	8404
1285	GGAACUCC U AGCCGCUU	1005	AAGCGGCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGUCC	8405
1289	CUCCUAGC C GCUUGUUU	1006	AAACAAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUAGGAG	8406
1292	CUAGCCGC U UGUUUUGC	1007	GCAAAACA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGCUAG	8407
1301	UGUUUUGC U CGCAGCAG	1008	CUGCUGCG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAAAACA	8408
1305	UUGCUCGC A GCAGGUCU	1009	AGACCUGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGAGCAA	8409
1308	CUCGCAGC A GGUCUGGG	1010	CCCAGACC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUGCGAG	8410
1313	AGCAGGUC U GGGGCAAA	1011	UUUGCCCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACCUGCU	8411
1319	UCUGGGGC A AAACUCAU	1012	AUGAGUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCCCAGA	8412
1324	GGCAAAAC U CAUCGGGA	1013	UCCCGAUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUUGCC	8413
1326	CAAAACUC A UCGGGACU	1014	AGUCCCGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUUUUG	8414
1334	AUCGGGAC U GACAAUUC	1015	GAAUUGUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCCGAU	8415
1338	GGACUGAC A AUUCUGUC	1016	GACAGAAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCAGUCC	8416
1343	GACAAUUC U GUCGUGCU	1017	AGCACGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAUUGUC	8417
1351	UGUCGUGC U CUCCCGCA	1018	UGC GGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICACGACA	8418
1353	UCGUGCUC U CCCGCAAA	1019	UUUGCGGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGCACGA	8419
1355	GUGCUCUC C CGCAAAUA	1020	UAUUUGCG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGAGCAC	8420
1356	UGCUCUCC C GCAAAUAU	1021	AUAUUUGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGAGCA	8421
1359	UCUCCGC A AAUAUACA	1022	UGUAUAUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGGAGA	8422
1367	AAAUUAC A UCAUUUCC	1023	GGAAUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUAUUU	8423
1370	UAUACAUC A UUUCCAUG	1024	CAUGGAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUUAUA	8424
1375	AUCAUUUC C AUGGCUGC	1025	GCAGCAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAUGAU	8425
1376	UCAUUUCC A UGCUGCU	1026	AGCAGCCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAUGA	8426
1381	UCCAUGGC U GCUAGGCU	1027	AGCCUAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCAUGGA	8427
1384	AUGGCUGC U AGGUGUG	1028	CACAGCCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGCAU	8428
1389	UGCUGGC U GUGCUGCC	1029	GGCAGCAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCUAGCA	8429
1394	GGCUGUGC U GCCAACUG	1030	CAGUUGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICACAGCC	8430
1397	UGUGCUGC C AACUGGAU	1031	AUCCAGUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGACA	8431
1398	GUGCUGCC A ACUGGAUC	1032	UAUCCAGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCAGCAC	8432
1401	CUGCCAAC U GGAUCCUA	1033	UAGGAUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGCCAG	8433
1407	ACUGGAUC C UACGCGGG	1034	CCCGGUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUCCAGU	8434
1408	CUGGAUCC U ACGCGGGA	1035	UCCCGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAUCCAG	8435
1421	GGGACGUC C UUGUUUA	1036	UAAACAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACGUCCC	8436
1422	GGACGUCC U UUGUUUAC	1037	GUAAACAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGACGUCC	8437
1434	UUUACGUC C CGUCGGCG	1038	CGCCGACG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACGUAAA	8438
1435	UUACGUCC C GUCGGCGC	1039	GCGCCGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGACGUAA	8439
1444	GUCGGCGC U GAAUCCCG	1040	CGGGAUUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGCCGAC	8440
1450	GCUGAAUC C CGCGGACG	1041	CGUCCGCG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUUCAGC	8441
1451	CUGAAUCC C GCGGACGA	1042	UCGUCCGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAUUCAG	8442
1461	CGGACGAC C CUCCCCG	1043	CCGGGAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCGUCCG	8443
1462	GGAGACC C CUCCCCGG	1044	CCCGGGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUCGUCC	8444
1463	GACGACCC C UCCCGGGG	1045	CCCCGGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGUCGUC	8445
1464	ACGACCCC U CCCGGGGC	1046	GCCCCGGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGGUCGU	8446
1466	GACCCUC C CGGGGCCG	1047	CGGCCCCG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGGGUC	8447
1467	ACCCUCC C GGGGCCGC	1048	GCGGCCCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGGGGU	8448
1473	CCCGGGGC C GCUUGGGG	1049	CCCCAAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCCCGGG	8449
1476	GGGGCCGC U UGGGGCUC	1050	GAGCCCCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGCCCC	8450
1483	CUUGGGGC U CUACCGCC	1051	GGCGGUAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCCCAAG	8451
1485	UGGGGCUC U ACCGCCG	1052	CGGGCGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGCCCCA	8452
1488	GGCUCUAC C GCCGCUU	1053	AAGCGGCG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUAGAGCC	8453

1491	UCUACCGC C CGCUUCUC	1054	GAGAAGCG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGUAGA	8454
1492	CUACCGCC C GCUUCUCC	1055	GGAGAAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGUAG	8455
1495	CCGCCC GC U UCUCGCC	1056	GGCGGAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGCGG	8456
1498	CCCGCUUC U CCGCCUAU	1057	AUAGGCGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGCGGG	8457
1500	CGCUUCUC C GCCUAUUG	1058	CAAUAGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGAAGCG	8458
1503	UUCUCCGC C UAUUGUAC	1059	GUACAAUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGAGAA	8459
1504	UCUCCGCC U AUUGUACC	1060	GGUACAAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGAGAA	8460
1512	UAUUGUAC C GACCGUCC	1061	GGACGGUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUACAAUA	8461
1516	GUACCGAC C GUCCACGG	1062	CCGUGGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCGGUAC	8462
1520	CGACCGUC C ACGGGGCG	1063	CGCCCCGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACGGUCG	8463
1521	GACCGUCC A CGGGGCGC	1064	GCGCCCCG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGACGGUC	8464
1530	CGGGGCGC A CCUCUCUU	1065	AAGAGAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGCCCCG	8465
1532	GGGCGCAC C UCUCUUUA	1066	UAAAGAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGCGCCC	8466
1533	GGCGCACC U CUCUUUAC	1067	GUAAAGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGCGCC	8467
1535	CGCACCUC U CUUUACGC	1068	GCGUAAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGUGCG	8468
1537	CACCUCUC U UUACGCGG	1069	CCGCGUAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGAGGUG	8469
1548	ACGCGGAC U CCCCUCU	1070	AGACGGGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCGCGU	8470
1550	GCGGACUC C CCGUCUGU	1071	ACAGACGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUCCGC	8471
1551	CGGACUCC C CGUCUGUG	1072	CACAGACG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGUCCG	8472
1552	GGACUCCC C GUCUGUGC	1073	GCACAGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGAGUCC	8473
1556	UCCCCGUC U GUGCCUUC	1074	GAAGGCAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACGGGGA	8474
1561	GUCUGUGC C UUCUCAUC	1075	GAUGAGAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICACAGAC	8475
1562	UCUGUGCC U UCUCAUCU	1076	AGAUGAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCACAGA	8476
1565	GUGCCUUC U CAUCUGCC	1077	GGCAGAUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGGCAC	8477
1567	GCCUUCUC A UCUGCCGG	1078	CCGGCAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGAAGGC	8478
1570	UUCUCAUC U GCCGACC	1079	GGUCCGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUGAGAA	8479
1573	UCAUCUGC C GGACCGUG	1080	CACGGUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGAUGA	8480
1578	UGCCGGAC C GUGUGCAC	1081	GUGCACAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCGGCA	8481
1585	CCGUGUGC A CUUCGCUU	1082	AAGCGAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICACACGG	8482
1587	GUGUGCAC U UCGCUUCA	1083	UGAAGCGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGCACAC	8483
1592	CACUUCGC U UCACCUCU	1084	AGAGGUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGAAGUG	8484
1595	UUCGUUUC A CCUCUGCA	1085	UGCAGAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGCGAA	8485
1597	CGCUUCAC C UCUGCACG	1086	CGUGCAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGAAGCG	8486
1598	GCUUCACC U CUGCACGU	1087	ACGUGCAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGAAGC	8487
1600	UUCACCUC U GCACGUCG	1088	CGACGUGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGUGAA	8488
1603	ACCUCUGC A CGUCGCAU	1089	AUGCGACG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGAGGU	8489
1610	CACGUCGC A UGGAGACC	1090	GGUCUCCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGACGUG	8490
1618	AUGGAGAC C ACCGUGAA	1091	UUCACGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCUCCAU	8491
1619	UGGAGACC A CCGUGAAC	1092	GUUCACGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUCUCCA	8492
1621	GAGACCAC C GUGAACGC	1093	GCGUUCAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGUCUC	8493
1630	GUGAACGC C CACAGGAA	1094	UUCUGUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGUUCAC	8494
1631	UGAACGCC C ACAGGAAC	1095	GUUCCUGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGGUUCA	8495
1632	GAACGCC A CAGGAACC	1096	GGUCCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGCGUUC	8496
1634	ACGCCAC A GGAACCUG	1097	CAGGUUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGCGU	8497
1640	ACAGGAAC C UGCCCAAG	1098	CUUGGGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCCUGU	8498
1641	CAGGAACC U GCCCAAGG	1099	CCUUGGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUCCUG	8499
1644	GAACUGC C CAAGGUCU	1100	AGACCUUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGUUC	8500
1645	AACUGCC C AAGGUCU	1101	AAGACCUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCAGGUU	8501
1646	ACCUGCCC A AGGUCUUG	1102	CAAGACCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGCAGGU	8502
1652	CCAAGGUC U UGCAUAAG	1103	CUUAUGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACCUUGG	8503
1656	GGUCUUGC A UAAGAGGA	1104	UCCUCUUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAAGACC	8504

1666	AAGAGGAC U CUUGGACU	1105	AGUCCAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCUCUU	8505
1668	GAGGACUC U UGGACUUU	1106	AAAGUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUCCUC	8506
1674	UCUUGGAC U UUCAGCAA	1107	UUGCUGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCAAGA	8507
1678	GGACUUUC A GCAAUGUC	1108	GACAUUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAAGUCC	8508
1681	CUUUCAGC A AUGUCAAC	1109	GUUGACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUGAAAG	8509
1687	GCAAUGUC A ACGACCGA	1110	UCGGUCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACAUUGC	8510
1693	UCAACGAC C GACCUUGA	1111	UCAAGGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCGUUGA	8511
1697	CGACCGAC C UUGAGGCA	1112	UGCCUCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCGGUCG	8512
1698	GACCGACC U UAGGCAU	1113	AUGCCUCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUCGGUC	8513
1705	CUUGAGGC A UACUUCAA	1114	UUGAAGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCUCAAG	8514
1709	AGGCAUAC U UCAAAGAC	1115	GUCUUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAUGCCU	8515
1712	CAUACUUC A AAGACUGU	1116	ACAGUCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGUAUG	8516
1718	UCAAGAC U GUGUGUUU	1117	AAACACAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCUUUGA	8517
1769	UAAAGGUC U UUGUACUA	1118	UAGUACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACCUUUA	8518
1776	CUUUGUAC U AGGAGGCU	1119	AGCCUCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUACAAAG	8519
1784	UAGGAGGC U GUAGGCAU	1120	AUGCCUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCUCCUA	8520
1791	CUGUAGGC A UAAAUUGG	1121	CCAAUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCUACAG	8521
1807	GUGUGUUC A CCAGCACC	1122	GGUGCUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAACACAC	8522
1809	GUGUUCAC C AGCACCAU	1123	AUGGUGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGAACAC	8523
1810	UGUUCACC A GCACCAUG	1124	CAUGGUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGAACA	8524
1813	UCACCAGC A CCAUGCAA	1125	UUGCAUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUGGUGA	8525
1815	ACCAGCAC C AUGCAACU	1126	AGUUGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGCUGGU	8526
1816	CCAGCACC A UGCAACUU	1127	AAGUUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGCUGG	8527
1820	CACCAUGC A ACUUUUUC	1128	GAAAAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAUGGUG	8528
1823	CAUGCAAC U UUUUACAC	1129	GGUGAAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGCAUG	8529
1829	ACUUUUUC A CCUCUGCC	1130	GGCAGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAAAAGU	8530
1831	UUUUUCAC C UCUGCCUA	1131	UAGGCAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGAAAAA	8531
1832	UUUUCACC U CUGCCUAA	1132	UUAGGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGAAAA	8532
1834	UUCACCUC U GCCUAAUC	1133	GAUUAGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGUGAA	8533
1837	ACCUCUGC C UAAUCAUC	1134	GAUGAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGAGGU	8534
1838	CCUCUGCC U AAUCAUCU	1135	AGAUGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAGAGG	8535
1843	GCCUAAUC A UCUCAUGU	1136	ACAUGAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUAGGC	8536
1846	UAAUCAUC U CAUGUUCA	1137	UGAACAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUAUUA	8537
1848	AUCAUCUC A UGUUCAUG	1138	CAUGAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAUGAU	8538
1854	UCAUGUUC A UGUCCUAC	1139	GUAGGACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAACAUGA	8539
1859	UUCAUGUC C UACUGUUC	1140	GAACAGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACAUGAA	8540
1860	UCAUGUCC U ACUGUUCA	1141	UGAACAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGACAUGA	8541
1863	UGUCCUAC U GUUCAAGC	1142	GCUUGAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAGGACA	8542
1868	UACUGUUC A AGCCUCCA	1143	UGGAGGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAACAGUA	8543
1872	GUUCAAGC C UCCAAGCU	1144	AGCUUGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUUGAAC	8544
1873	UUCAAGCC U CCAAGCUG	1145	CAGCUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCUUGAA	8545
1875	CAAGCCUC C AAGCUGUG	1146	CACAGCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGCUUG	8546
1876	AAGCCUCC A AGCUGUGC	1147	GCACAGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGGCUU	8547
1880	CUCCAAGC U GUGCCUUG	1148	CAAGGCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUUGGAG	8548
1885	AGCUGUGC C UUGGGUGG	1149	CCACCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICACAGCU	8549
1886	GCUGUGCC U UGGGUGGC	1150	GCCACCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCACAGC	8550
1895	UGGGUGGC U UUGGGGCA	1151	UGCCCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCACCCA	8551
1903	UUUGGGGC A UGGACAUU	1152	AAUGUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCCAAA	8552
1909	GCAUGGAC A UUGACCCG	1153	CGGGUCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCAUGC	8553
1915	ACAUGAC C CGUAUAAA	1154	UUUAUACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCAAUGU	8554
1916	CAUUGACC C GUUAAAAG	1155	CUUUAUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUCAAUG	8555

1935	UUUGGAGC U UCUGUGGA	1156	UCCACAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUCCAAA	8556
1938	GGAGCUUC U GUGGAGUU	1157	AACUCCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGCUCC	8557
1949	GGAGUUAC U CUCUUUUU	1158	AAAAAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAACUCC	8558
1951	AGUUACUC U CUUUUUUG	1159	CAAAAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUAACU	8559
1953	UUACUCUC U UUUUUGCC	1160	GGCAAAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAGUAA	8560
1961	UUUUUUGC C UUCUGACU	1161	AGUCAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAAAAA	8561
1962	UUUUUGCC U UCUGACUU	1162	AAGUCAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAAAAA	8562
1965	UUGCCUUC U GACUUCUU	1163	AAGAAGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGGCAA	8563
1969	CUUCUGAC U UCUUUCCU	1164	AGGAAAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCAGAAG	8564
1972	CUGACUUC U UUCUUUCU	1165	AGAAGGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGUCAG	8565
1976	CUUCUUUC C UUCUAUUC	1166	GAAUAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAAGAAG	8566
1977	UUCUUUCC U UCUAUUCG	1167	CGAAUAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAAAGAA	8567
1980	UUUCCUUC U AUUCGAGA	1168	UCUCGAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGGAAA	8568
1991	UCGAGAUC U CCUCGACA	1169	UGUCGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUCUGA	8569
1993	GAGAUUC C UCGACACC	1170	GGUGUCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAUCUC	8570
1994	AGAUCUCC U CGACACCG	1171	CGGUGUCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGAUCU	8571
1999	UCCUCGAC A CCGCCUCU	1172	AGAGGCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCGAGGA	8572
2001	CUCGACAC C GCCUCUGC	1173	GCAGAGGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGUCGAG	8573
2004	GACACCGC C UCUGCUCU	1174	AGAGCAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGUGUC	8574
2005	ACACCGCC U CUGCUCUG	1175	CAGAGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGUGU	8575
2007	ACCGCUC U GCUCUGUA	1176	UACAGAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGCGGU	8576
2010	GCCUCUGC U CUGUAUCG	1177	CGAUACAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGAGGC	8577
2012	CUCUGCUC U GUUACGGG	1178	CCC GAUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGCAGAG	8578
2025	CGGGGGGC C UUAGAGUC	1179	GACUCUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCCCG	8579
2026	GGGGGGCC U UAGAGUCU	1180	AGACUCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCCCC	8580
2034	UUAGAGUC U CCGGAACA	1181	UGUUCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACUCUAA	8581
2036	AGAGUCUC C GGAACAUU	1182	AAUGUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGACUCU	8582
2042	UCCGGAAC A UUGUUCAC	1183	GUGAACAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUCCGGA	8583
2049	CAUUGUUC A CCUCACCA	1184	UGGUGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAACAAUG	8584
2051	UUGUUCAC C UCACCAUA	1185	UAUGGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGAACAA	8585
2052	UGUUCACC U CACCAUAC	1186	GUAUGGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGAACAA	8586
2054	UUCACCUC A CCAUACGG	1187	CCGUUAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGUGAA	8587
2056	CACCUCAC C AUACGGCA	1188	UGCCGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGAGGUG	8588
2057	ACCUCACC A UACGGCAC	1189	GUGCCGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGAGGU	8589
2064	CAUACGGC A CUCAGGCA	1190	UGCCUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCGUAUG	8590
2066	UACGGCAC U CAGGCAAG	1191	CUUGCCUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGCCGUA	8591
2068	CGGCACUC A GGCAAGCU	1192	AGCUUGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUGCCG	8592
2072	ACUCAGGC A AGCUAUUC	1193	GAAUAGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCUGAGU	8593
2076	AGGCAAGC U AUUCUGUG	1194	CACAGAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUUGCCU	8594
2081	AGCUAUUC U GUGUUGGG	1195	CCCAACAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUAGCU	8595
2105	GAUGAAUC U AGCCACCU	1196	AGGUGGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUCAUC	8596
2109	AAUCUAGC C ACCUGGGU	1197	ACCCAGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUAGAUU	8597
2110	AUCUAGCC A CCUGGGUG	1198	CACCCAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCUAGAU	8598
2112	CUAGCCAC C UGGGUGGG	1199	CCCACCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGGCUAG	8599
2113	UAGCCACC U GGGUGGGA	1200	UCCACCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGGCUA	8600
2138	GGAAGAU C AGCAUCCA	1201	UGGAUGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUCUUCC	8601
2139	GAAGAUCC A GCAUCCAG	1202	CUGGAUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUCUUC	8602
2142	GAUCCAGC A UCCAGGGA	1203	UCCUGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUGGAUC	8603
2145	CCAGCAUC C AGGGAAUU	1204	AAUUCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUGCUGG	8604
2146	CAGCAUCC A GGGAAUUA	1205	UAAUCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUGCUG	8605
2161	UAGUAGUC A GCUAUGUC	1206	GACAUAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IACUACUA	8606

2164	UAGUCAGC U AUGUCAAC	1207	GUUGACAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUGACUA	8607
2170	GCUAUGUC A ACGUUAU	1208	AUUAACGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACAUAGC	8608
2185	AUAUGGGC C UAAAAAUC	1209	GAUUUUUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCCAUAU	8609
2186	UAUGGGCC U AAAAAUCA	1210	UGAUUUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCCCAUA	8610
2194	UAAAAAUC A GACAACUA	1211	UAGUUGUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUUUUUA	8611
2198	AAUCAGAC A ACUAUUGU	1212	ACAAUAGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCUGAUU	8612
2201	CAGACAAC U AUUGUGGU	1213	ACCACAAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGUCUG	8613
2213	GUGGUUUC A CAUUUCCU	1214	AGGAAAUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAACCAC	8614
2215	GGUUUCAC A UUUCUGU	1215	ACAGGAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGAAACC	8615
2220	CACAUUUC C UGUCUAC	1216	GUAAGACA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAUGUG	8616
2221	ACAUUUC C UGUUACU	1217	AGUAAGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAAAUGU	8617
2225	UUCUGUC U UACUUUUG	1218	CAAAUGUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACAGGAA	8618
2229	UGUCUAC U UUUGGGCG	1219	CGCCAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUAAGACA	8619
2244	CGAGAAAC U GUUCUUGA	1220	UCAAGAAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUCUCG	8620
2249	AACUGUUC U UGAAUAU	1221	AAUAUUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAAGUUU	8621
2265	UUGGUGUC U UUUGGAGU	1222	ACUCCAAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACACCAA	8622
2284	GGAUUCGC A CUCCUCCU	1223	AGGAGGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGAAUCC	8623
2286	AUUCGCAC U CCUCCUGC	1224	GCAGGAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGCGAAU	8624
2288	UCGCACUC C UCCUGCAU	1225	AUGCAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUGCGA	8625
2289	CGCACUCC U CCUGCAUA	1226	UAUGCAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGUGCG	8626
2291	CACUCCUC C UGCAUAUA	1227	UAUAUGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGAGUG	8627
2292	ACUCCUCC U GCAUAUAG	1228	CUAUAUGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGGAGU	8628
2295	CCUCCUGC A UAUAGACC	1229	GGUCUAUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGAGG	8629
2303	AUAUAGAC C ACCAAUUG	1230	CAUUUGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCUAUAU	8630
2304	UAUAGACC A CCAAUUGC	1231	GCAUUUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUCUAUA	8631
2306	UAGACCAC C AAAUGCCC	1232	GGGCAUUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGUCUA	8632
2307	AGACCACC A AAUGCCCC	1233	GGGGCAUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGGUCU	8633
2313	CCAAUUGC C CCUAUCUU	1234	AAGAUAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAUUUGG	8634
2314	CAAUUGCC C CUAUCUUA	1235	UAAGAUAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCAUUUG	8635
2315	AAUUGCCC C UAUCUUAU	1236	AUAAGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGCAUUU	8636
2316	AAUGCCCC U AUCUUAUC	1237	GAUAAGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGGCAUU	8637
2320	CCCCUAUC U UAACAACA	1238	UGUUGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUAGGGG	8638
2325	AUCUUAUC A ACACUCC	1239	GGAUGUGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUAGAUU	8639
2328	UUAUCAAC A CUUCCGGA	1240	UCCGGAAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUGAUAA	8640
2330	AUCAACAC U UCCGGAUA	1241	UUUCCGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGUUGAU	8641
2333	AACACUUC C GGAAACUA	1242	UAGUUUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAAGUGUU	8642
2340	CCGGAAAC U ACUGUUGU	1243	ACAACAGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUUCGCG	8643
2343	GAAACUAC U GUUGUUG	1244	CUAACAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUAGUUUC	8644
2362	GAAGAGGC A GGUCCCCU	1245	AGGGGACC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCUCUUC	8645
2367	GGCAGGUC C CCUAGAAG	1246	CUUCUAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACCUGCC	8646
2368	GCAGGUCC C CUAGAAGA	1247	UCUUCUAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGACCUGC	8647
2369	CAGGUCCC C UAGAAGAA	1248	UUCUUCUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGACCUG	8648
2370	AGGUCCCC U AGAAGAAG	1249	CUUCUUCU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGGACCU	8649
2382	AGAAGAAC U CCCUCGCC	1250	GGCGAGGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUUCUUCU	8650
2384	AAGAACUC C CUCGCCUC	1251	GAGGCGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUUCUU	8651
2385	AGAACUCC C UCGCCUCG	1252	CGAGGCGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGUUCU	8652
2386	GAACUCCC U CGCCUCGC	1253	GCGAGGCG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGAGUUC	8653
2390	UCCUCGCG C UCGCAGAC	1254	GUCUGCGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGAGGGA	8654
2391	CCCUCGCC U CGCAGACG	1255	CGUCUGCG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGAGGGG	8655
2395	CGCCUCGC A GACGAAGG	1256	CCUUCGUC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICGAGGCG	8656
2406	CGAAGGUC U CAAUCGCC	1257	GGCGAUUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IACCUUCG	8657

2408	AAGGUCUC A AUCGCCGC	1258	GCGGCGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGACCUU	8658
2414	UCAAUCGC C GCGUCGCA	1259	UGCGACGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGAUUGA	8659
2422	CGCGUCGC A GAAGAUCU	1260	AGAUCUUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGACGCG	8660
2430	AGAAGAUC U CAAUCUCG	1261	CGAGAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUCUCU	8661
2432	AAGAUCUC A AUCUCGGG	1262	CCCAGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGAUCUU	8662
2436	UCUCAAUC U CGGGAUUC	1263	GAUUCCTG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUGAGA	8663
2445	CGGGAUUC U CAAUGUUA	1264	UAACAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUCCTG	8664
2447	GGAUCUC A AUGUUGU	1265	ACUAACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUUC	8665
2460	UAGUAUUC C UUGGACAC	1266	GUGUCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUACUA	8666
2461	AGUAUUC U UGGACACA	1267	UGUGUCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAAUACU	8667
2467	CCUUGGAC A CAUAAGGU	1268	ACCUUAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCAAGG	8668
2469	UUGGACAC A UAAGGUGG	1269	CCACGUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGUCCAA	8669
2483	UGGGAUAC U UUACGGGG	1270	CCCCGUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUCCCA	8670
2493	UACGGGGC U UUAUUCUU	1271	AAGAAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCCGUA	8671
2500	CUUUAUUC U UCUCGGU	1272	ACCGUAGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUAAAG	8672
2503	UAUUCUUC U ACGGUACC	1273	GGUACCGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGAAUA	8673
2511	UACGGUAC C UUGCUUUA	1274	UAAAGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUACCGUA	8674
2512	ACGGUACC U UGCUUUA	1275	UUAAGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUACCGU	8675
2516	UACCUUGC U UUAUCCU	1276	AGGAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAGGUA	8676
2523	CUUAAUUC C UAAUUGG	1277	GCCAUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUAAAG	8677
2524	UUUAAUCC U AAUUGGCA	1278	UGCCAUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUUA	8678
2532	UAAUUGG A AACUCCUU	1279	AAGGAGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCAUUUA	8679
2536	UGGCAAAC U CCUUCUUU	1280	AAAGAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUGCCA	8680
2538	GCAAACUC C UUCUUUUC	1281	GAAAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUUUGC	8681
2539	CAAACUCC U UCUUUUC	1282	GGAAAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGUUUG	8682
2542	ACUCCUUC U UUUCCUGA	1283	UCAGGAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAGGAGU	8683
2547	UUCUUUUC C UGACAUUC	1284	GAAUGUCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAAAGAA	8684
2548	UCUUUUC C UGACAUUC	1285	UGAAUGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAAAGAA	8685
2552	UUCUGAC A UUAUUUG	1286	CAAUGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCAGGAA	8686
2556	UGACAUUC A UUGCAGG	1287	CCUGCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUGUCA	8687
2562	UCAUUUGC A GGAGACA	1288	UGUCCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAUGA	8688
2570	AGGAGGAC A UUGUUGAU	1289	AUCAACA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCUCCU	8689
2589	AUGUAAGC A AUUUGUGG	1290	CCACAAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUUAU	8690
2601	UGUGGGGC C CCUACAG	1291	CUGUAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCCACA	8691
2602	GUGGGGCC C CUACAGU	1292	ACUGUAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCCCAC	8692
2603	UGGGGGCC C UACAGUA	1293	UACUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGCCCCA	8693
2604	GGGGCCCC U UACAGUA	1294	UUAUGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGGGCCC	8694
2608	CCCCUAC A GUAAUGA	1295	UCAUUUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAAGGGG	8695
2621	AUGAAAC A GGAGACU	1296	AAGUCUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUUUCAU	8696
2628	CAGGAGAC U UAAUUUA	1297	UUAAUUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCUCCUG	8697
2638	AAAUUAC U AUGCCUGC	1298	GCAGGCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUAUUU	8698
2643	AACUAUGC C UGUAGGU	1299	ACCUAGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAUAGU	8699
2644	ACUAUGCC U GCUAGGU	1300	AACCUAGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAUAGU	8700
2647	AUGCCUGC U AGGUUUUA	1301	UAAACCUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGGCAU	8701
2658	GUUUUAC C CAAUGUUA	1302	UAAAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUAAAAC	8702
2659	UUUUAUCC C AAUGUUAC	1303	GUAAAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUAAAA	8703
2660	UUUAUCCC A AUGUUACU	1304	AGUAACAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGAUAAA	8704
2668	AAUGUUAC U AAUUAUU	1305	AAAUUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAACAUU	8705
2679	AUAUUUGC C CUAGAUU	1306	UAUCUAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAAAU	8706
2680	UAUUUGCC C UUAUAUA	1307	UUUUCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCAAAU	8707
2681	AUUUGCCC U UAGAUAA	1308	UUUAUCUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGCAAAU	8708

2696	AAGGGAUC A AACCGUAU	1309	AUACGGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUCCCUU	8709
2700	GAUCAAAC C GUUUUAUC	1310	GAUAAUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUUGAUC	8710
2709	GUUUUAUC C AGAGUAUG	1311	CAUACUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUAAUAC	8711
2710	UAUUUAUC A GAGUAUGU	1312	ACAUACUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAUAUA	8712
2727	AGUUAAUC A UUAUUUCC	1313	GGAAGUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUUAAUCU	8713
2732	AUCAUUAC U UCCAGACG	1314	CGUCUGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUAUAUGAU	8714
2735	AUUACUUC C AGACGCGA	1315	UCGCGUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAGUAAU	8715
2736	UUACUUCC A GACGCGAC	1316	GUCGCGUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAAGUAA	8716
2745	GACGCGAC A UUAUUUAC	1317	GUAAAUAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUCGCGUC	8717
2754	UUUUUAUC A CACUCUUU	1318	AAAGAGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUAAAUAA	8718
2756	AUUUACAC C CUUUUGG	1319	CCAAAGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGUAAAU	8719
2758	UUACACAC U CUUUGGAA	1320	UUCCAAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGUGUAA	8720
2760	ACACACUC U UUGGAAGG	1321	CCUUCCAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAGUGUGU	8721
2777	CGGGGAUC U UAUUAUAA	1322	UUUAUAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUCCCCG	8722
2794	AGAGAGUC C ACACGUAG	1323	CUACGUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACUCUCU	8723
2795	GAGAGUCC A CACGUAGC	1324	GCUACGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACUCUCU	8724
2797	GAGUCCAC A CGUAGCGC	1325	GCGCUACG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGGACUC	8725
2806	CGUAGCGC C UCAUUUUG	1326	CAAAUAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICGCUACG	8726
2807	GUAGCGCC U CAUUUUGC	1327	GCAAAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGCGCUAC	8727
2809	AGCGCCUC A UUUUGCGG	1328	CCGCAAAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAGGCGCU	8728
2821	UGCGGGUC A CCAUAUUC	1329	GAAUAUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACCCGCA	8729
2823	CGGGUCAC C AUAUUCUU	1330	AAGAAUUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUGACCCG	8730
2824	GGGUCACC A UAUUCUUG	1331	CAAGAAUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGUGACCC	8731
2830	CCAUAUUC U UGGGAACA	1332	UGUUCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUAUUGG	8732
2838	UUGGGAAC A AGAUCUAC	1333	GUAGAUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUCCCAA	8733
2844	ACAAGAUC U ACAGCAUG	1334	CAUGCUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUCUUGU	8734
2847	AGAUCUAC A GCAUGGGA	1335	UCCCAUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUAGAUCU	8735
2850	UCUACAGC A UGGGAGGU	1336	ACCUCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICUGUAGA	8736
2864	GGUUGGUC U UCCAAACC	1337	GGUUUGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACCAACC	8737
2867	UGGUCUUC C AAACCUCG	1338	CGAGGUUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAGACCA	8738
2868	GGUCUUC C AACCUCGA	1339	UCGAGGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAAGACC	8739
2872	UUCCAAAC C UCGAAAAG	1340	CUUUUCGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUUUGGAA	8740
2873	UCCAAACC U CGAAAAGG	1341	CCUUUUCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGUUUGGA	8741
2883	GAAAAGGC A UGGGAGCA	1342	UGUCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	ICCUUUUC	8742
2891	AUGGGGAC A AAUCUUUC	1343	GAAAGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IUCCCAU	8743
2896	GACAAUUC U UUCUGUCC	1344	GGACAGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUUUGUC	8744
2900	AAUCUUUC U GUCCCCAA	1345	UUGGGGAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAAGAUU	8745
2904	UUUCUGUC C CCAAUCCC	1346	GGGAUUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IACAGAAA	8746
2905	UUCUGUCC C CAAUCCCC	1347	GGGGAUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGACAGAA	8747
2906	UCUGUCCC C AAUCCCCU	1348	AGGGGAUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGACAGA	8748
2907	CUGUCCCC A AUCCCCUG	1349	CAGGGGAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGGACAG	8749
2911	CCCCAAUC C CCUGGGAU	1350	AUCCCAAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUUGGGG	8750
2912	CCCCAUCC C CUGGGAUU	1351	AAUCCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAUGGGG	8751
2913	CCAAUCCC C UGGGAUUC	1352	GAAUCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGAUUGG	8752
2914	CAAUCCCC U GGAUUCU	1353	AGAAUCCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGGAUUG	8753
2922	UGGGAUUC U UCCCCGAU	1354	AUCGGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAUCCCA	8754
2925	GAUUCUUC C CCGAUCAU	1355	AUGAUCGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAAGAAUC	8755
2926	AUUCUUC C CGAUCAUC	1356	GAUGAUCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGAAGAAU	8756
2927	UUCUUC C GAUCAUCA	1357	UGAUGAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IGGAAGAA	8757
2932	CCCCGAUC A UCAGUUGG	1358	CCAACUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUCGGGG	8758
2935	CGAUCAUC A GUUGGACC	1359	GGUCCAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA	IAUGAUCG	8759

2943	AGUUGGAC C CUGCAUUC	1360	GAAUGCAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCAACU	8760
2944	GUUGGACC C UGCAUUCA	1361	UGAAUGCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUCCAAC	8761
2945	UUGGACCC U GCAUUCAA	1362	UUGAAUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGUCCAA	8762
2948	GACCCUGC A UUCAAAAGC	1363	GCUUUGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICAGGGUC	8763
2952	CUGCAUUC A AAGCCAAC	1364	GUUGGCUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAAUGCAG	8764
2957	UUCAAGC C AACUCAGU	1365	ACUGAGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUUUGAA	8765
2958	UCAAGCC A ACUCAGUA	1366	UACUGAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCUUUGA	8766
2961	AAGCCAAC U CAGUAAAU	1367	AUUUACUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGGCUU	8767
2963	GCCAACUC A GUAAAUC	1368	GGAUUUAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUUGGC	8768
2971	AGUAAAUC C AGAUUGGG	1369	CCCAAUCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAUUUACU	8769
2972	GUAAAUC C GAUUGGGA	1370	UCCCAAUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAUUUAC	8770
2982	AUUGGGAC C UCAACCCG	1371	CGGGUUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCCAAU	8771
2983	UUGGGACC U CAACCCGC	1372	GCGGGUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUCCCAA	8772
2985	GGGACCUC A ACCCGCAC	1373	GUGCGGGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGUCCC	8773
2988	ACCUCAAC C CGCACAAG	1374	CUUGUGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGAGGU	8774
2989	CCUCAACC C GCACAAGG	1375	CCUUGUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGUAGG	8775
2992	CAACCCGC A CAAGGACA	1376	UGUCCUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGGUUG	8776
2994	ACCCGCAC A AGGACAAC	1377	GUUGUCCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGCGGGU	8777
3000	ACAAGGAC A ACUGGCCG	1378	CGGCCAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCUUGU	8778
3003	AGGACAAC U GGCCGGAC	1379	GUCCGGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGUCCU	8779
3007	CAACUGGC C GGACCCA	1380	UGGCGUCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCAGUUG	8780
3014	CCGGACGC C AACAAGGU	1381	ACCUUGUU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGUCCGG	8781
3015	CGGACGCC A ACAAGGUG	1382	CACCUUGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGGUCCG	8782
3018	ACGCCAAC A AGGUGGGA	1383	UCCCACCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGGCGU	8783
3035	GUGGGAGC A UUCGGGCC	1384	GGCCCGAA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUCCAC	8784
3043	AUUCGGGC C AGGGUUA	1385	UGAACCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCCGAAU	8785
3044	UUCGGGCC A GGGUUCAC	1386	GUGAACCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCCGAA	8786
3051	CAGGGUUC A CCCUCCC	1387	GGGAGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAACCCUG	8787
3053	GGGUUCAC C CUCCCCA	1388	UGGGGAGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGAACCC	8788
3054	GGUUCACC C CUCCCCAU	1389	AUGGGGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGUGAAC	8789
3055	GUUCACCC C UCCCAUG	1390	CAUGGGGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGUGAAC	8790
3056	UUCACCCC U CCCAUGG	1391	CCAUGGGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGUGAA	8791
3058	CACCCUC C CCAUGGG	1392	CCCCAUGG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGGGUG	8792
3059	ACCCUCC C CAUGGGG	1393	CCCCAUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGAGGGG	8793
3060	CCCUCCC C AUGGGGA	1394	UCCCCAU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGAGGG	8794
3061	CCCUCCC A UGGGGAC	1395	GUCCCCA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGAGGG	8795
3070	UGGGGGAC U GUUGGGU	1396	ACCCCAAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUCCCCA	8796
3084	GGUGGAGC C CUCACGU	1397	AGCGUGAG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICUCCACC	8797
3085	GUGGAGCC C UCACGCUC	1398	GAGCGUGA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCUCAC	8798
3086	UGGAGCCC U CACGCUA	1399	UGAGCGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGGUCCA	8799
3088	GAGCCUC A CGCUCAGG	1400	CCUGAGCG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGGGCUC	8800
3092	CCUCACGC U CAGGGCCU	1401	AGGCCUC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICGUGAGG	8801
3094	UCACGCUC A GGGCCUAC	1402	GUAGGCC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGCGUGA	8802
3099	CUCAGGGC C UACUCACA	1403	UGUGAGUA CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICCUGAG	8803
3100	UCAGGGCC U ACUCACAA	1404	UUGUGAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCCUGA	8804
3103	GGGCCUAC U CACAACUG	1405	CAGUUGUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUAGGCC	8805
3105	GCCUACUC A CAACUGUG	1406	CACAGUUG CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IAGUAGG	8806
3107	CUACUCAC A ACUGUGCC	1407	GGCACAGU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUGAGUAG	8807
3110	CUCACAAC U GUGCCAGC	1408	GCUGGCAC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IUUGUGAG	8808
3115	AACUGUGC C AGCAGCUC	1409	GAGCUGCU CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA ICACAGUU	8809
3116	ACUGUGCC A GCAGCUC	1410	GGAGCUGC CUGAUGAG	<u>GCCGUUAGGC</u>	CGAA IGCACAGU	8810

3119	GUGCCAGC A GCUCCUCC	1411	GGAGGAGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUGGCAC	8811
3122	CCAGCAGC U CCUCCUCC	1412	GGAGGAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUGCUGG	8812
3124	AGCAGCUC C UCCUCCUG	1413	CAGGAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGCUGCU	8813
3125	GCAGCUC U CCUCCUGC	1414	GCAGGAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGCUGC	8814
3127	AGCUCUCC C UCCUGCCU	1415	AGGCAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGAGCU	8815
3128	GCUCCUCC U CCUGCCUC	1416	GAGGCAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGGAGC	8816
3130	UCCUCCUC C UGCCUCCA	1417	UGGAGGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGAGGA	8817
3131	CCUCCUCC U GCCUCCAC	1418	GUGGAGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGGAGG	8818
3134	CCUCCUGC C UCCACCAA	1419	UUGGUGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICAGGAGG	8819
3135	CUCUCCG C CCACCAAU	1420	AUUGGUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCAGGAG	8820
3137	CCUGCCUC C ACCAAUCG	1421	CGAUUGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGCAGG	8821
3138	CUGCCUCC A CCAAUCGG	1422	CCGAUUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGGCAG	8822
3140	GCCUCCAC C AAUCGGCA	1423	UGCCGAUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGAGGC	8823
3141	CCUCCACC A AUCGGCAG	1424	CUGCCGAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGGAGG	8824
3148	CAAUCGGC A GUCAGGAA	1425	UUCUGAC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCGAUUG	8825
3152	CGGCAGUC A GGAAGGCA	1426	UGCCUCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCUCCG	8826
3160	AGGAAGGC A GCCUACUC	1427	GAGUAGGC CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCUCCU	8827
3163	AAGGCAGC C UACUCCCU	1428	AGGGAGUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICUGCCUU	8828
3164	AGGCAGCC U ACUCCCUU	1429	AAGGGAGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCUGCCU	8829
3167	CAGCCUAC U CCCUUAUC	1430	GAUAAGGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUAGGCUG	8830
3169	GCCUACUC C CUUAUCUC	1431	GAGAUAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUAGGC	8831
3170	CCUACUCC C UUAUCUCC	1432	GGAGAUAA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGUAGG	8832
3171	CUACUCCC U UAUCUCCA	1433	UGGAGUA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGGAGUAG	8833
3176	CCCUUAUC U CCACCUCU	1434	AGAGGUGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUAGGG	8834
3178	CUUAUCUC C ACCUCUAA	1435	UUAGAGGU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGAUAA	8835
3179	UUAUCUCC A CCUCUAA	1436	CUUAGAGG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAGUAA	8836
3181	AUCUCCAC C UCUAAGGG	1437	CCCUUAGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGGAGAU	8837
3182	UCUCCACC U CUAAGGGA	1438	UCCCUUAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGUGGAGA	8838
3184	UCCACCUC U AAGGGACA	1439	UGUCCCUU CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGUGGA	8839
3192	UAAGGGAC A CUCAUCCU	1440	AGGAUGAG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUCCCUUA	8840
3194	AGGGACAC U CAUCCUCA	1441	UGAGGAUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IUGUCCCU	8841
3196	GGACACUC A UCCUCAGG	1442	CCUGAGGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGUGUCC	8842
3199	CACUCAUC C UCAGGCCA	1443	UGGCCUGA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAUGAGUG	8843
3200	ACUCAUCC U CAGGCCAU	1444	AUGGCCUG CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGAUGAGU	8844
3202	UCAUCCUC A GGCCAUGC	1445	GCAUGGCC CUGAUGAG <u>GCCGUUAGGC</u> CGAA IAGGAUGA	8845
3206	CCUCAGGC C AUGCAGUG	1446	CACUGCAU CUGAUGAG <u>GCCGUUAGGC</u> CGAA ICCUGAGG	8846
3207	CUCAGGCC A UGCAGUGG	1447	CCACUGCA CUGAUGAG <u>GCCGUUAGGC</u> CGAA IGCCUGAG	8847

Input Sequence = AF100308. Cut Site = CH/.

Stem Length = 8 . Core Sequence = CUGAUGAG X CGAA (X = GCCGUUAGGC or other stem II)

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

Underlined region can be any X sequence or linker, as described herein.

"I" stands for Inosine

TABLE VII: HUMAN HBV G-CLEAVER AND SUBSTRATE SEQUENCE

Pos	Substrate	Seq ID	G-cleaver	Seq ID
61	ACUUUCCU G CUGGUGGC	1448	GCCACCAG UGAUG GCAUGCACUAUGC GCG AGGAAAGU	8848
87	GGAACAGU G AGCCUCG	1449	GCAGGGCU UGAUG GCAUGCACUAUGC GCG ACUGUUC	8849
94	UGAGCCCU G CUCAGAAU	1450	AUUCUGAG UGAUG GCAUGCACUAUGC GCG AGGGCUCA	8850
112	CUGUCUCU G CCAUAUCG	1451	CGAUUAGG UGAUG GCAUGCACUAUGC GCG AGAGACAG	8851
132	AUCUUAUC G AAGACUGG	1452	CCAGUCUU UGAUG GCAUGCACUAUGC GCG GAUAAGAU	8852
153	CCUGUACC G AACAUUGA	1453	UCCAUGUU UGAUG GCAUGCACUAUGC GCG GGUACAGG	8853
169	AGAACAUC G CAUCAGGA	1454	UCCUGAUG UGAUG GCAUGCACUAUGC GCG GAUGUUCU	8854
192	GGACCCCU G CUCGUGUU	1455	AACACGAG UGAUG GCAUGCACUAUGC GCG AGGGGUCC	8855
222	UUCUUGUU G AAAAAAU	1456	AUUUUGU UGAUG GCAUGCACUAUGC GCG AACAGAA	8856
315	CAAAAUUC G CAGUCCCA	1457	UGGGACUG UGAUG GCAUGCACUAUGC GCG GAAUUUUG	8857
374	UGGUUAUC G CUGGAUGU	1458	ACAUCCAG UGAUG GCAUGCACUAUGC GCG GAUAACCA	8858
387	AUGUGUCU G CGGCGUUU	1459	AAACGCCG UGAUG GCAUGCACUAUGC GCG AGACACAU	8859
410	CUUCCUCU G CAUCCUGC	1460	GCAGGAUG UGAUG GCAUGCACUAUGC GCG AGAGGAAG	8860
417	UGCAUCCU G CUGCUAUG	1461	CAUAGCAG UGAUG GCAUGCACUAUGC GCG AGGAGUCA	8861
420	AUCCUGCU G CUAUGCCU	1462	AGGCAUAG UGAUG GCAUGCACUAUGC GCG AGCAGGAU	8862
425	GCUGCUAU G CCUCAUCU	1463	AGAUGAGG UGAUG GCAUGCACUAUGC GCG AUAGCAGC	8863
468	GGUAUGUU G CCCGUUUG	1464	CAACCGG UGAUG GCAUGCACUAUGC GCG AACAUACC	8864
518	CGGACCAU G CAAAACCU	1465	AGGUUUUG UGAUG GCAUGCACUAUGC GCG AUGGUCCG	8865
527	CAAAACCU G CACAACUC	1466	GAGUUGUG UGAUG GCAUGCACUAUGC GCG AGGUUUUG	8866
538	CAACUCCU G CUCAAGGA	1467	UCCUUGAG UGAUG GCAUGCACUAUGC GCG AGGAGUUG	8867
569	CUCAUGUU G CUGUACAA	1468	UUGUACAG UGAUG GCAUGCACUAUGC GCG AACAUAGAG	8868
596	CGGAAACU G CACCUGUA	1469	UACAGGUG UGAUG GCAUGCACUAUGC GCG AGUUUCCG	8869
631	GGGCUUUC G CAAAUAUC	1470	GUUUUUUG UGAUG GCAUGCACUAUGC GCG GAAAGCCC	8870
687	UUACUAGU G CCAUUUGU	1471	ACAAAUGG UGAUG GCAUGCACUAUGC GCG ACUAGUAA	8871
747	AUAUGGAU G AUGUGGUU	1472	AACCACAU UGAUG GCAUGCACUAUGC GCG AUCCAUAU	8872
783	AACAUCUU G AGUCCCUU	1473	AAGGGACU UGAUG GCAUGCACUAUGC GCG AAGAUGUU	8873
795	CCCUUUUAU G CCGCUGUU	1474	AACAGCGG UGAUG GCAUGCACUAUGC GCG AUAAAAGG	8874
798	UUUAUGCC G CUGUUACC	1475	GGUAACAG UGAUG GCAUGCACUAUGC GCG GGCAUAAA	8875
911	GGCACAUI G CCACAGGA	1476	UCCUGUGG UGAUG GCAUGCACUAUGC GCG AAUGUGCC	8876
978	GGCCUAUU G AAUGGAAA	1477	UUUCCAAU UGAUG GCAUGCACUAUGC GCG AAUAGGCC	8877
997	AUGUCAAC G AAUUGUGG	1478	CCACAAU UGAUG GCAUGCACUAUGC GCG GUUGACAU	8878
1020	UGGGGUUU G CCGCCCCU	1479	AGGGGCGG UGAUG GCAUGCACUAUGC GCG AAACCCCA	8879
1023	GGUUUGCC G CCCCUIUC	1480	GAAAGGGG UGAUG GCAUGCACUAUGC GCG GGCAAAACC	8880
1034	CCUUUCAC G CAAUGUGG	1481	CCACAUUG UGAUG GCAUGCACUAUGC GCG GUGAAAGG	8881
1050	GAUAUUCU G CUUUAUUG	1482	CAUUAAG UGAUG GCAUGCACUAUGC GCG AGAAUAUC	8882
1058	GCUUUAAU G CCUUUAUA	1483	UAUAAAGG UGAUG GCAUGCACUAUGC GCG AUUAAAGC	8883
1068	CUUUUAUAU G CAUGCAUA	1484	UAUGCAUG UGAUG GCAUGCACUAUGC GCG AUUAUAAAG	8884
1072	AUAUGCAU G CAUACAAG	1485	CUUGUAUG UGAUG GCAUGCACUAUGC GCG AUGCAUAU	8885
1103	ACUUUCUC G CCAACUUA	1486	UAAGUUGG UGAUG GCAUGCACUAUGC GCG GAGAAAGU	8886
1139	CAGUAUGU G AACCUUUA	1487	UAAAGGUU UGAUG GCAUGCACUAUGC GCG ACAUACUG	8887
1155	ACCCCGUU G CUCGGCAA	1488	UUGCCGAG UGAUG GCAUGCACUAUGC GCG AACGGGGU	8888
1177	UGGUCUAU G CCAAGUGU	1489	ACACUUGG UGAUG GCAUGCACUAUGC GCG AUAGACCA	8889
1188	AAGUGUUU G CUGACGCA	1490	UGCGUCAG UGAUG GCAUGCACUAUGC GCG AAACACUU	8890
1191	UGUUUGCU G ACGCAACC	1491	GGUUGCGU UGAUG GCAUGCACUAUGC GCG AGCAAACA	8891
1194	UUGCUGAC G CAACCCCC	1492	GGGGGUUG UGAUG GCAUGCACUAUGC GCG GUCAGCAA	8892
1234	CCAUCAGC G CAUGCGUG	1493	CACGCAUG UGAUG GCAUGCACUAUGC GCG GCUGAUGG	8893
1238	CAGCGCAU G CGUGGAAC	1494	GUUCCACG UGAUG GCAUGCACUAUGC GCG AUGCGCUG	8894

1262	UCUCCUCU G CCGAUCCA	1495	UGGAUCGG UGAUG GCAUGCACUAUGC GCG AGAGGAGA	8895
1265	CCUCUGCC G AUCCAUAAC	1496	GUAUGGAU UGAUG GCAUGCACUAUGC GCG GGCAGAGG	8896
1275	UCCAUACC G CGGAACUC	1497	GAGUUCGG UGAUG GCAUGCACUAUGC GCG GGUAUGGA	8897
1290	UCCUAGCC G CUUGUUUU	1498	AAAACAAG UGAUG GCAUGCACUAUGC GCG GGCUAGGA	8898
1299	CUUGUUUU G CUCGCAGC	1499	GCUGCGAG UGAUG GCAUGCACUAUGC GCG AAAACAAG	8899
1303	UUUUGCUC G CAGCAGGU	1500	ACCUGCUG UGAUG GCAUGCACUAUGC GCG GAGCAAAA	8900
1335	UCGGGACU G ACAAUUCU	1501	AGAAUUGU UGAUG GCAUGCACUAUGC GCG AGUCCCGA	8901
1349	UCUGUCGU G CUCUCCCG	1502	CGGGAGAG UGAUG GCAUGCACUAUGC GCG ACGACAGA	8902
1357	GCUCUCCC G CAAAUUAU	1503	UAUAUUUG UGAUG GCAUGCACUAUGC GCG GGGAGAGC	8903
1382	CCAUGGCU G CUAGGCUG	1504	CAGCCUAG UGAUG GCAUGCACUAUGC GCG AGCCAUGG	8904
1392	UAGGCUGU G CUGCCAAC	1505	GUUGGCAG UGAUG GCAUGCACUAUGC GCG ACAGCCUA	8905
1395	GCUGUGCU G CCAACUGG	1506	CCAGUUGG UGAUG GCAUGCACUAUGC GCG AGCACAGC	8906
1411	GAUCCUAC G CGGGACGU	1507	ACGUCCCG UGAUG GCAUGCACUAUGC GCG GUAGGAUC	8907
1442	CCGUCGGC G CUGAAUCC	1508	GGAGUCAG UGAUG GCAUGCACUAUGC GCG GCCGACGG	8908
1445	UCGGCGCU G AAUCCCGC	1509	GCGGGAUU UGAUG GCAUGCACUAUGC GCG AGCGCCGA	8909
1452	UGAAUCCC G CGGACGAC	1510	GUCGUCCG UGAUG GCAUGCACUAUGC GCG GGGUAUCA	8910
1458	CCGCGGAC G ACCCCUCC	1511	GGAGGGGU UGAUG GCAUGCACUAUGC GCG GUCCGCGG	8911
1474	CCGGGGCC G CUUGGGGC	1512	GCCCCAAG UGAUG GCAUGCACUAUGC GCG GGCCCCGG	8912
1489	GCUCUACC G CCCGCUUC	1513	GAAGCGGG UGAUG GCAUGCACUAUGC GCG GGUAGAGC	8913
1493	UACCGCCC G CUUCUCCG	1514	CGGAGAAG UGAUG GCAUGCACUAUGC GCG GGGCGGUA	8914
1501	GCUUCUCC G CCUAUUGU	1515	ACAAUAGG UGAUG GCAUGCACUAUGC GCG GGAGAAGC	8915
1513	AUUGUACC G ACCGUCCA	1516	UGGACGGU UGAUG GCAUGCACUAUGC GCG GGUACAAU	8916
1528	CACGGGGC G CACCUCUC	1517	GAGAGGUG UGAUG GCAUGCACUAUGC GCG GCCCCGUG	8917
1542	CUCUUUAC G CGGACUCC	1518	GGAGUCCG UGAUG GCAUGCACUAUGC GCG GUAAAGAG	8918
1559	CCGUCUGU G CCUUCUCA	1519	UGAGAAGG UGAUG GCAUGCACUAUGC GCG ACAGACGG	8919
1571	UCUCAUCU G CCGGACCG	1520	CGGUCCGG UGAUG GCAUGCACUAUGC GCG AGAUGAGA	8920
1583	GACCUGUG G CACUUCGC	1521	GCGAAGUG UGAUG GCAUGCACUAUGC GCG ACACGGUC	8921
1590	UGCACUUC G CUUCACCU	1522	AGGUGAAG UGAUG GCAUGCACUAUGC GCG GAAGUGCA	8922
1601	UCACCUCU G CACGUCGC	1523	GCGACGUG UGAUG GCAUGCACUAUGC GCG AGAGGUGA	8923
1608	UGCACGUC G CAUGGAGA	1524	UCUCCAUG UGAUG GCAUGCACUAUGC GCG GACGUGCA	8924
1624	ACCACCGU G AACGCCCA	1525	UGGGCGUU UGAUG GCAUGCACUAUGC GCG ACGGUGGU	8925
1628	CCGUGAAC G CCCACAGG	1526	CCUGUGGG UGAUG GCAUGCACUAUGC GCG GUUCACGG	8926
1642	AGGAACCU G CCCAAGGU	1527	ACCUUGGG UGAUG GCAUGCACUAUGC GCG AGGUUCCU	8927
1654	AAGGUCUU G CAUAAGAG	1528	CUCUUAUG UGAUG GCAUGCACUAUGC GCG AAGACCUU	8928
1690	AUGUCAAC G ACCGACCU	1529	AGGUCGGU UGAUG GCAUGCACUAUGC GCG GUUGACAU	8929
1694	CAACGACC G ACCUUGAG	1530	CUCAAGGU UGAUG GCAUGCACUAUGC GCG GGUCGUUG	8930
1700	CCGACCUU G AGGCAUAC	1531	GUAUGCCU UGAUG GCAUGCACUAUGC GCG AAGGUCGG	8931
1730	UGUUUAAU G AGUGGGAG	1532	CUCCCAU UGAUG GCAUGCACUAUGC GCG AUUAAACA	8932
1818	AGCACCAU G CAACUUUU	1533	AAAAGUUG UGAUG GCAUGCACUAUGC GCG AUGGUGCU	8933
1835	UCACCUCU G CCUAAUCA	1534	UGAUUAGG UGAUG GCAUGCACUAUGC GCG AGAGGUGA	8934
1883	CAAGCUGU G CCUUGGGU	1535	ACCCAAGG UGAUG GCAUGCACUAUGC GCG ACAGCUUG	8935
1912	UGGACAUU G ACCCGUAU	1536	AUACGGGU UGAUG GCAUGCACUAUGC GCG AAUGUCCA	8936
1959	UCUUUUUU G CCUUCUGA	1537	UCAGAAGG UGAUG GCAUGCACUAUGC GCG AAAAAAGA	8937
1966	UGCCUUCU G ACUUCUUU	1538	AAAGAAGU UGAUG GCAUGCACUAUGC GCG AGAAGGCA	8938
1985	UUCUAUUC G AGAUCUCC	1539	GGAGAUCU UGAUG GCAUGCACUAUGC GCG GAAUAGAA	8939
1996	AUCUCCUC G ACACCGCC	1540	GGCGGUGU UGAUG GCAUGCACUAUGC GCG GAGGAGAU	8940
2002	UCGACACC G CCUCUGCU	1541	AGCAGAGG UGAUG GCAUGCACUAUGC GCG GGUGUCGA	8941
2008	CCGCCUCU G CUCUGUAU	1542	AUACAGAG UGAUG GCAUGCACUAUGC GCG AGAGGCGG	8942
2092	GUUGGGGU G AGUUGAUG	1543	CAUCAACU UGAUG GCAUGCACUAUGC GCG ACCCCAAC	8943
2097	GGUGAGUU G AUGAAUCU	1544	AGAUUCAU UGAUG GCAUGCACUAUGC GCG AACUCACC	8944
2100	GAGUUGAU G AAUCUAGC	1545	GCUAGAUU UGAUG GCAUGCACUAUGC GCG AUCAACUC	8945

2237	UUUUGGGC G AGAAACUG	1546	CAGUUUCU UGAUG GCAUGCACUAUGC GCG GCCCAAAA	8946
2251	CUGUUCUU G AAUAUUUG	1547	CAAAUAUU UGAUG GCAUGCACUAUGC GCG AAGAACAG	8947
2282	GUGGAUUC G CACUCCUC	1548	GAGGAGUG UGAUG GCAUGCACUAUGC GCG GAAUCCAC	8948
2293	CUCCUCCU G CAUAUAGA	1549	UCUAUAUG UGAUG GCAUGCACUAUGC GCG AGGAGGAG	8949
2311	CACCAAAU G CCCCUAUC	1550	GAUAGGGG UGAUG GCAUGCACUAUGC GCG AUUUGGUG	8950
2354	UGUUAGAC G AAGAGGCA	1551	UGCCUCUU UGAUG GCAUGCACUAUGC GCG GUCUAACA	8951
2388	ACUCCUC G CCUCGCAG	1552	CUGCGAGG UGAUG GCAUGCACUAUGC GCG GAGGGAGU	8952
2393	CUCGCCUC G CAGACGAA	1553	UUCGUCUG UGAUG GCAUGCACUAUGC GCG GAGGCGAG	8953
2399	UCGCAGAC G AAGGUCUC	1554	GAGACCUU UGAUG GCAUGCACUAUGC GCG GUCUGCGA	8954
2412	UCUCAAUC G CCGCGUCG	1555	CGACGCGG UGAUG GCAUGCACUAUGC GCG GAUUGAGA	8955
2415	CAAUCGCC G CGUCGCAG	1556	CUGCGACG UGAUG GCAUGCACUAUGC GCG GGC GAUUG	8956
2420	GCCGCGUC G CAGAAGAU	1557	AUCUUCUG UGAUG GCAUGCACUAUGC GCG GACGCGGC	8957
2514	GGUACCUU G CUUUAUUC	1558	GAUUAAG UGAUG GCAUGCACUAUGC GCG AAGGUACC	8958
2549	CUUUUCCU G ACAUUAU	1559	AUGAAUGU UGAUG GCAUGCACUAUGC GCG AGGAAAAG	8959
2560	AUUCAUUU G CAGGAGGA	1560	UCCUCCUG UGAUG GCAUGCACUAUGC GCG AAUUGAAU	8960
2576	ACAUUGUU G AUAGAUGU	1561	ACAUUAU UGAUG GCAUGCACUAUGC GCG AACAAUGU	8961
2615	CAGUAAAU G AAAACAGG	1562	CCUGUUUU UGAUG GCAUGCACUAUGC GCG AUUUACUG	8962
2641	UUAACUAU G CCUGCUAG	1563	CUAGCAGG UGAUG GCAUGCACUAUGC GCG AUAGUUA	8963
2645	CUAUGCCU G CUAGGUUU	1564	AAACCUAG UGAUG GCAUGCACUAUGC GCG AGGCAUAG	8964
2677	AAAUUUU G CCUUAAGA	1565	UCUAAGGG UGAUG GCAUGCACUAUGC GCG AAUAUUU	8965
2740	UUCAGAC G CGACAUUA	1566	UAAUGUCG UGAUG GCAUGCACUAUGC GCG GUCUGGAA	8966
2742	CCAGACGC G ACAUUAUU	1567	AAUAUGU UGAUG GCAUGCACUAUGC GCG GCGUCUGG	8967
2804	CACGUAGC G CCUCAUUU	1568	AAAUGAGG UGAUG GCAUGCACUAUGC GCG GCUACGUG	8968
2814	CUCAUUUU G CGGGUCAC	1569	GUGACCCG UGAUG GCAUGCACUAUGC GCG AAAAUGAG	8969
2875	CAAAACCUC G AAAAGGCA	1570	UGCCUUUU UGAUG GCAUGCACUAUGC GCG GAGGUUUG	8970
2928	UCUCCCC G AUCAUCAG	1571	CUGAUGAU UGAUG GCAUGCACUAUGC GCG GGGGAAGA	8971
2946	UGGACCCU G CAUUCAAA	1572	UUUGAAUG UGAUG GCAUGCACUAUGC GCG AGGGUCCA	8972
2990	CUCAACCC G CACAAGGA	1573	UCCUUGUG UGAUG GCAUGCACUAUGC GCG GGGUUGAG	8973
3012	GGCCGGAC G CCAACAAG	1574	CUUGUUGG UGAUG GCAUGCACUAUGC GCG GUCCGGCC	8974
3090	GCCUCAC G CUCAGGGC	1575	GCCCUGAG UGAUG GCAUGCACUAUGC GCG GUGAGGGC	8975
3113	ACAACUGU G CCAGCAGC	1576	GCUGCUGG UGAUG GCAUGCACUAUGC GCG ACAGUUGU	8976
3132	CUCCUCCU G CCUCCACC	1577	GGUGGAGG UGAUG GCAUGCACUAUGC GCG AGGAGGAG	8977
51	AGGGCCCU G UACUUUCC	1578	GGAAAGUA UGAUG GCAUGCACUAUGC GCG AGGGCCCU	8978
106	AGAAUACU G UCUCUGCC	1579	GGCAGAGA UGAUG GCAUGCACUAUGC GCG AGUUAUUCU	8979
148	GGGACCCU G UACCGAAC	1580	GUUCGGUA UGAUG GCAUGCACUAUGC GCG AGGGUCCC	8980
198	CUGCUCGU G UUACAGGC	1581	GCCUGUAA UGAUG GCAUGCACUAUGC GCG ACGAGCAG	8981
219	UUUUUCUU G UUGACAAA	1582	UUUGUCAA UGAUG GCAUGCACUAUGC GCG AAGAAAAA	8982
297	ACACCCGU G UGUCUUGG	1583	CCAAGACA UGAUG GCAUGCACUAUGC GCG ACGGGUGU	8983
299	ACCCGUGU G UCUUGGCC	1584	GGCCAAGA UGAUG GCAUGCACUAUGC GCG ACACGGGU	8984
347	ACCAACCU G UUGUCCUC	1585	GAGGACAA UGAUG GCAUGCACUAUGC GCG AGGUUGGU	8985
350	AACCUGUU G UCCUCCAA	1586	UUGGAGGA UGAUG GCAUGCACUAUGC GCG AACAGGUU	8986
362	UCCAAUUU G UCCUGGUU	1587	AACCAGGA UGAUG GCAUGCACUAUGC GCG AAUUGGA	8987
381	CGCUGGAU G UGUCUGCG	1588	CGCAGACA UGAUG GCAUGCACUAUGC GCG AUCCAGCG	8988
383	CUGGAUGU G UCUGCGGC	1589	GCCGCAGA UGAUG GCAUGCACUAUGC GCG ACAUCCAG	8989
438	AUCUUCUU G UUGGUUCU	1590	AGAACCAA UGAUG GCAUGCACUAUGC GCG AAGAAGAU	8990
465	CAAGGUAU G UUGCCCGU	1591	ACGGGCAA UGAUG GCAUGCACUAUGC GCG AUACCUUG	8991
476	GCCCGUUU G UCCUCUAA	1592	UUAGAGGA UGAUG GCAUGCACUAUGC GCG AAACGGGC	8992
555	ACCUCUAU G UUUCCUC	1593	GAGGGAAA UGAUG GCAUGCACUAUGC GCG AUAGAGGU	8993
566	UCCUCUAU G UUGCUGUA	1594	UACAGCAA UGAUG GCAUGCACUAUGC GCG AUGAGGGA	8994
572	AUGUUGCU G UACAAAC	1595	GUUUUGUA UGAUG GCAUGCACUAUGC GCG AGCAACAU	8995
602	CUGCACCU G UAUUCCCA	1596	UGGAAUA UGAUG GCAUGCACUAUGC GCG AGGUGCAG	8996

694	UGCCAUUU G UUCAGUGG	1597	CCACUGAA UGAUG GCAUGCACUAUGC GCG AAAUGGCA	8997
724	CCCCCACU G UCUGGCUU	1598	AAGCCAGA UGAUG GCAUGCACUAUGC GCG AGUGGGGG	8998
750	UGGAUGAU G UGGUUUUG	1599	CAAAACCA UGAUG GCAUGCACUAUGC GCG AUCAUCCA	8999
771	CCAAGUCU G UACAACAU	1600	AUGUUGUA UGAUG GCAUGCACUAUGC GCG AGACUUGG	9000
801	AUGCCGCU G UUACCAAU	1601	AUUGGUAA UGAUG GCAUGCACUAUGC GCG AGCGGCAU	9001
818	UUUCUUUU G UCUUUGGG	1602	CCCAAAGA UGAUG GCAUGCACUAUGC GCG AAAAGAAA	9002
888	UGGGAUUAU G UAAUUGGG	1603	CCCAAUUA UGAUG GCAUGCACUAUGC GCG AUAUCCCA	9003
927	AACAUUAU G UACAAAAA	1604	UUUUUGUA UGAUG GCAUGCACUAUGC GCG AAUAUGUU	9004
944	AUCAAAAU G UGUUUUAG	1605	CUAAAACA UGAUG GCAUGCACUAUGC GCG AUUUUGAU	9005
946	CAAAAUGU G UUUUAGGA	1606	UCCUAAAA UGAUG GCAUGCACUAUGC GCG ACAUUUUG	9006
963	AACUUCU G UAAACAGG	1607	CCUGUUUA UGAUG GCAUGCACUAUGC GCG AGGAAGUU	9007
991	GAAAGUAU G UCAACGAA	1608	UUCGUUGA UGAUG GCAUGCACUAUGC GCG AUACUUUC	9008
1002	AACGAAUU G UGGGUCUU	1609	AAGACCCA UGAUG GCAUGCACUAUGC GCG AAUUCGUU	9009
1039	CACGCAAU G UGGAUAUU	1610	AAUAUCCA UGAUG GCAUGCACUAUGC GCG AUUGCGUG	9010
1137	AACAGUAU G UGAACCUU	1611	AAGGUUCA UGAUG GCAUGCACUAUGC GCG AUACUGUU	9011
1184	UGCCAAGU G UUUGCUGA	1612	UCAGCAAA UGAUG GCAUGCACUAUGC GCG ACUUGGCA	9012
1251	GAACCUUU G UGUCUCCU	1613	AGGAGACA UGAUG GCAUGCACUAUGC GCG AAAGGUUC	9013
1253	ACCUUUGU G UCUCUCU	1614	AGAGGAGA UGAUG GCAUGCACUAUGC GCG ACAAGGUU	9014
1294	AGCCGCUU G UUUUGCUC	1615	GAGCAAAA UGAUG GCAUGCACUAUGC GCG AAGCGGCU	9015
1344	ACAAUUCU G UCGUGCUC	1616	GAGCACGA UGAUG GCAUGCACUAUGC GCG AGAAUUGU	9016
1390	GCUAGGCU G UGUGCCA	1617	UGGCAGCA UGAUG GCAUGCACUAUGC GCG AGCCUAGC	9017
1425	CGUCCUUU G UUUACGUC	1618	GACGUAAA UGAUG GCAUGCACUAUGC GCG AAAGGACG	9018
1508	CGCCUAUU G UACCGACC	1619	GGUCGGUA UGAUG GCAUGCACUAUGC GCG AAUAGGCG	9019
1557	CCCCGUCU G UGCCUUCU	1620	AGAAGGCA UGAUG GCAUGCACUAUGC GCG AGACGGGG	9020
1581	CGGACCGU G UGCACUUC	1621	GAAGUGCA UGAUG GCAUGCACUAUGC GCG ACGGUCCG	9021
1684	UCAGCAAU G UCAACGAC	1622	GUCGUUGA UGAUG GCAUGCACUAUGC GCG AUUGCUGA	9022
1719	CAAAGACU G UGUGUUUA	1623	UAAACACA UGAUG GCAUGCACUAUGC GCG AGUCUUUG	9023
1721	AAGACUGU G UGUUUAAU	1624	AUUAAACA UGAUG GCAUGCACUAUGC GCG ACAGUCUU	9024
1723	GACUGUGU G UUUAAUGA	1625	UCAUUAAA UGAUG GCAUGCACUAUGC GCG ACACAGUC	9025
1772	AGGUCUUU G UACUAGGA	1626	UCCUAGUA UGAUG GCAUGCACUAUGC GCG AAAGACCU	9026
1785	AGGAGGCU G UAGGCAUA	1627	UAUGCCUA UGAUG GCAUGCACUAUGC GCG AGCCUCCU	9027
1801	AAAUUGGU G UGUUCACC	1628	GGUGAACA UGAUG GCAUGCACUAUGC GCG ACCAAUUU	9028
1803	AUUGGUGU G UUCACCAG	1629	CUGUGAAA UGAUG GCAUGCACUAUGC GCG ACACCAAU	9029
1850	CAUCUCAU G UUCAUGUC	1630	GACAUGAA UGAUG GCAUGCACUAUGC GCG AUGAUGAU	9030
1856	AUGUJCAU G UCCUACUG	1631	CAGUAGGA UGAUG GCAUGCACUAUGC GCG AUGAACAU	9031
1864	GUCCUACU G UUCAAGCC	1632	GGCUUGAA UGAUG GCAUGCACUAUGC GCG AGUAGGAC	9032
1881	UCCAAGCU G UGCCUUGG	1633	CCAAGGCA UGAUG GCAUGCACUAUGC GCG AGCUUGGA	9033
1939	GAGCUUCU G UGGAGUUA	1634	UAACUCCA UGAUG GCAUGCACUAUGC GCG AGAAGCUC	9034
2013	UCUGCUCU G UAUCGGGG	1635	CCCCGAUA UGAUG GCAUGCACUAUGC GCG AGAGCAGA	9035
2045	GGAACAUU G UUCACCUC	1636	GAGGUGAA UGAUG GCAUGCACUAUGC GCG AAUGUUC	9036
2082	GCUAUUCU G UGUUGGGG	1637	CCCCAACA UGAUG GCAUGCACUAUGC GCG AGAAUAGC	9037
2084	UAUUCUGU G UUGGGGUG	1638	CACCCCAA UGAUG GCAUGCACUAUGC GCG ACAGAAUA	9038
2167	UCAGCUAU G UCAACGUU	1639	AACGUUGA UGAUG GCAUGCACUAUGC GCG AUAGCUGA	9039
2205	CAACUAUU G UGGUUUCA	1640	UGAAACCA UGAUG GCAUGCACUAUGC GCG AAUAGUUG	9040
2222	CAUUUCCU G UCUUACUU	1641	AAGUAAGA UGAUG GCAUGCACUAUGC GCG AGGAAAUG	9041
2245	GAGAAACU G UUCUUGAA	1642	UUCAAGAA UGAUG GCAUGCACUAUGC GCG AGUUUCUC	9042
2262	UAUUUGGU G UCUUUUGG	1643	CCAAAAGA UGAUG GCAUGCACUAUGC GCG ACCAAAUA	9043
2274	UUUGGAGU G UGGAUUCG	1644	CGAAUCCA UGAUG GCAUGCACUAUGC GCG ACUCCAAA	9044
2344	AAACUACU G UUGUUAGA	1645	UCUAACAA UGAUG GCAUGCACUAUGC GCG AGUAGUUU	9045
2347	CUACUGUU G UUAGACGA	1646	UCGUCUAA UGAUG GCAUGCACUAUGC GCG AACAGUAG	9046
2450	AUCUCAAU G UUAGUAUU	1647	AAUACUAA UGAUG GCAUGCACUAUGC GCG AUUGAGAU	9047

MBHB02,249-E (400.042US)

2573	AGGACAUU G UUGAUAGA	1648	UCUAUCAA UGAUG GCAUGCACUAUGC GCG AAUGUCCU	9048
2583	UGAUAGAU G UAAGCAAU	1649	AUUGCUUA UGAUG GCAUGCACUAUGC GCG AUCUAUCA	9049
2594	AGCAAUUU G UGGGGCCC	1650	GGGCCCCA UGAUG GCAUGCACUAUGC GCG AAAUUGCU	9050
2663	AUCCCAAU G UUACUAAA	1651	UUUAGUAA UGAUG GCAUGCACUAUGC GCG AUUGGGAU	9051
2717	CAGAGUAU G UAGUUAU	1652	AUUAACUA UGAUG GCAUGCACUAUGC GCG AUACUCUG	9052
2901	AUCUUUCU G UCCCCAAU	1653	AUUGGGGA UGAUG GCAUGCACUAUGC GCG AGAAAGAU	9053
3071	GGGGGACU G UUGGGGUG	1654	CACCCCAA UGAUG GCAUGCACUAUGC GCG AGUCCCCC	9054
3111	UCACAACU G UGCCAGCA	1655	UGCUGGCA UGAUG GCAUGCACUAUGC GCG AGUUGUGA	9055

Input Sequence = AF100308. Cut Site = YG/M or UG/U.

Stem Length = 8. Core Sequence = UGAUG GCAUGCACUAUGC GCG

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

TABLE VIII: HUMAN HBV ZINZYME AND SUBSTRATE SEQUENCE

Pos	Substrate	Seq ID	Zinzyne	Seq ID
61	ACUUUCCU G CUGGUGGC	1448	GCCACCAG GCcgaagGCGaGuCaaGGuCu AGGAAAGU	9056
94	UGAGCCCU G CUCAGAAU	1450	AUUCUGAG GCcgaagGCGaGuCaaGGuCu AGGGCUCA	9057
112	CUGUCUCU G CCAUAUCG	1451	CGAUAUGG GCcgaagGCGaGuCaaGGuCu AGAGACAG	9058
169	AGAACAUC G CAUCAGGA	1454	UCCUGAUG GCcgaagGCGaGuCaaGGuCu GAUGUUCU	9059
192	GGACCCCU G CUCGUGUU	1455	AACACGAG GCcgaagGCGaGuCaaGGuCu AGGGGUCC	9060
315	CAAAAUUC G CAGUCCCA	1457	UGGGACUG GCcgaagGCGaGuCaaGGuCu GAAUUUUG	9061
374	UGGUUAUC G CUGGAUGU	1458	ACAUCCAG GCcgaagGCGaGuCaaGGuCu GAUAACCA	9062
387	AUGUGUCU G CGGCGUUU	1459	AAACGCCG GCcgaagGCGaGuCaaGGuCu AGACACAU	9063
410	CUUCCUCU G CAUCCUGC	1460	GCAGGAUG GCcgaagGCGaGuCaaGGuCu AGAGGAAG	9064
417	UGCAUCCU G CUGCUAUG	1461	CAUAGCAG GCcgaagGCGaGuCaaGGuCu AGGAUGCA	9065
420	AUCCUGCU G CUAUGCCU	1462	AGGCAUAG GCcgaagGCGaGuCaaGGuCu AGCAGGAU	9066
425	GCUGCUAU G CCUCAUCU	1463	AGAUGAGG GCcgaagGCGaGuCaaGGuCu AUAGCAGC	9067
468	GGUAUGUU G CCCGUUUG	1464	CAAACGGG GCcgaagGCGaGuCaaGGuCu AACAUACC	9068
518	CGGACCAU G CAAAACCU	1465	AGGUUUUG GCcgaagGCGaGuCaaGGuCu AUGGUCCG	9069
527	CAAAACCU G CACAACUC	1466	GAGUUGUG GCcgaagGCGaGuCaaGGuCu AGGUUUUG	9070
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596	CGGAAACU G CACCUGUA	1469	UACAGGUG GCcgaagGCGaGuCaaGGuCu AGUUUCCG	9073
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677	UUGGCUCA G UUUACUAG	1687	CUAGUAAA GCcgaagGCGaGuCaaGGuCu	UGAGCCAA	9258
685	GUUUACUA G UGCCAUUU	1688	AAAUGGCA GCcgaagGCGaGuCaaGGuCu	UAGUAAAC	9259
699	UUUGUUCA G UGGUUCGU	1689	ACGAACCA GCcgaagGCGaGuCaaGGuCu	UGAACAAA	9260
702	GUUCAGUG G UUCGUAGG	1690	CCUACGAA GCcgaagGCGaGuCaaGGuCu	CACUGAAC	9261
706	AGUGGUUC G UAGGGCUU	1691	AAGCCCUA GCcgaagGCGaGuCaaGGuCu	GAACCACU	9262
711	UUCGUAGG G CUUUCCCC	1692	GGGGAAAG GCcgaagGCGaGuCaaGGuCu	CCUACGAA	9263
729	ACUGUCUG G CUUUCAGU	1693	ACUGAAAG GCcgaagGCGaGuCaaGGuCu	CAGACAGU	9264
736	GGCUUUCA G UUAUAUGG	1694	CCAUUAUA GCcgaagGCGaGuCaaGGuCu	UGAAAGCC	9265
753	AUGAUGUG G UUUGGGG	1695	CCCCAAAA GCcgaagGCGaGuCaaGGuCu	CACAUCAU	9266
762	UUUUGGGG G CCAAGUCU	1696	AGACUUGG GCcgaagGCGaGuCaaGGuCu	CCCCAAAA	9267
767	GGGGCCAA G UCUGUACA	1697	UGUACAGA GCcgaagGCGaGuCaaGGuCu	UUGGCCCC	9268
785	CAUCUUGA G UCCCUUUA	1698	UAAAGGGA GCcgaagGCGaGuCaaGGuCu	UCAAGAUG	9269
826	GUCUUUGG G UAUACAUU	1699	AAUGUAUA GCcgaagGCGaGuCaaGGuCu	CCAAAGAC	9270
898	AAUUGGGA G UUGGGGCA	1700	UGCCCCAA GCcgaagGCGaGuCaaGGuCu	UCCCAAUU	9271
904	GAGUUGGG G CACAUUGC	1701	GCAUUGUG GCcgaagGCGaGuCaaGGuCu	CCCAACUC	9272
971	GUAAACAG G CCUAUUGA	1702	UCAAUAGG GCcgaagGCGaGuCaaGGuCu	CUGUUUAC	9273
987	AUUGGAAA G UAUGUCAA	1703	UUGACAUU GCcgaagGCGaGuCaaGGuCu	UUUCCAUA	9274
1006	AAUUGUGG G UCUUUUGG	1704	CCAAAAGA GCcgaagGCGaGuCaaGGuCu	CCACAAUU	9275
1016	CUUUUGGG G UUUGCCGC	1705	GCGGCAAA GCcgaagGCGaGuCaaGGuCu	CCCAAAAG	9276
1080	GCAUACAA G CAAAACAG	1706	CUGUUUUG GCcgaagGCGaGuCaaGGuCu	UUGUAUGC	9277
1089	CAAAACAG G CUUUUACU	1707	AGUAAAAG GCcgaagGCGaGuCaaGGuCu	CUGUUUUG	9278
1116	CUUACAAG G CCUUUCUA	1708	UAGAAAGG GCcgaagGCGaGuCaaGGuCu	CUUGUAAG	9279
1126	CUUUCUAA G UAAACAGU	1709	ACUGUUUA GCcgaagGCGaGuCaaGGuCu	UUAGAAAG	9280
1133	AGUAAACA G UAUGUGAA	1710	UUCACAUU GCcgaagGCGaGuCaaGGuCu	UGUUUACU	9281
1152	UUUACCCC G UUGCUCGG	1711	CCGAGCAA GCcgaagGCGaGuCaaGGuCu	GGGGUAAA	9282
1160	GUUGCUCG G CAACGGCC	1712	GGCCGUUG GCcgaagGCGaGuCaaGGuCu	CGAGCAAC	9283
1166	CGGCAACG G CCUGGUCU	1713	AGACCAGG GCcgaagGCGaGuCaaGGuCu	CGUUGCCG	9284
1171	ACGGCCUG G UCUAUGCC	1714	GGCAUAGA GCcgaagGCGaGuCaaGGuCu	CAGGCCGU	9285
1182	UAUGCCAA G UGUUUUCU	1715	AGCAAACA GCcgaagGCGaGuCaaGGuCu	UUGGCAUA	9286
1207	CCCCACUG G UUGGGGCU	1716	AGCCCCAA GCcgaagGCGaGuCaaGGuCu	CAGUGGGG	9287
1213	UGGUUGGG G CUUGGCCA	1717	UGGCCAAG GCcgaagGCGaGuCaaGGuCu	CCCAACCA	9288
1218	GGGGCUUG G CCAUAGGC	1718	GCCUAUGG GCcgaagGCGaGuCaaGGuCu	CAAGCCCC	9289
1225	GGCCAUAG G CCAUCAGC	1719	GCUGAUGG GCcgaagGCGaGuCaaGGuCu	CUAUGGCC	9290
1232	GGCCAUCA G CGCAUGCG	1720	CGCAUGCG GCcgaagGCGaGuCaaGGuCu	UGAUGGCC	9291
1240	GCGCAUGC G UGGAACCU	1721	AGGUUCCA GCcgaagGCGaGuCaaGGuCu	GCAUGCGC	9292
1287	AACUCCUA G CCGCUUGU	1722	ACAAGCGG GCcgaagGCGaGuCaaGGuCu	UAGGAGUU	9293
1306	UGCUCGCA G CAGGUCUG	1723	CAGACCUG GCcgaagGCGaGuCaaGGuCu	UGCGAGCA	9294
1310	CGCAGCAG G UCUGGGGC	1724	GCCCCAGA GCcgaagGCGaGuCaaGGuCu	CUGCUGCG	9295
1317	GGUCUGGG G CAAAACUC	1725	GAGUUUUG GCcgaagGCGaGuCaaGGuCu	CCCAGACC	9296
1347	AUUCUGUC G UGCUCUCC	1726	GGAGAGCA GCcgaagGCGaGuCaaGGuCu	GACAGAAU	9297
1379	UUUCCAUG G CUGCUAGG	1727	CCUAGCAG GCcgaagGCGaGuCaaGGuCu	CAUGGAAA	9298
1387	GCUGCUAG G CUGUGCUG	1728	CAGCACAG GCcgaagGCGaGuCaaGGuCu	CUAGCAGC	9299
1418	CGCGGGAC G UCCUUUGU	1729	ACAAAGGA GCcgaagGCGaGuCaaGGuCu	GUCCCGCG	9300
1431	UUGUUUAC G UCCCGUCG	1730	CGACGGGA GCcgaagGCGaGuCaaGGuCu	GUAAACAA	9301
1436	UACGUCCC G UCGGCGCU	1731	AGCGCCGA GCcgaagGCGaGuCaaGGuCu	GGGACGUA	9302
1440	UCCCGUCG G CGCUGAAU	1732	AUUCAGCG GCcgaagGCGaGuCaaGGuCu	CGACGGGA	9303
1471	CUCCCGGG G CCGCUUGG	1733	CCAAGCGG GCcgaagGCGaGuCaaGGuCu	CCCGGGAG	9304
1481	CGCUUGGG G CUCUACCG	1734	CGGUAGAG GCcgaagGCGaGuCaaGGuCu	CCCAAGCG	9305
1517	UACCGACC G UCCACGGG	1735	CCCUGGGA GCcgaagGCGaGuCaaGGuCu	GGUCGGUA	9306

1526	UCCACGGG G CGCACCUC	1736	GAGGUGCG GCcgaagGCGaGuCaaGGuCu CCCGUGGA	9307
1553	GACUCCCC G UCUGUGCC	1737	GGCACAGA GCcgaagGCGaGuCaaGGuCu GGGGAGUC	9308
1579	GCCGGACC G UGUGCACU	1738	AGUGCACACA GCcgaagGCGaGuCaaGGuCu GGUCCGGC	9309
1605	CUCUGCAC G UCGCAUGG	1739	CCAUGCGA GCcgaagGCGaGuCaaGGuCu GUGCAGAG	9310
1622	AGACCACC G UGAACGCC	1740	GGCGUUCA GCcgaagGCGaGuCaaGGuCu GGUGGUCU	9311
1649	UGCCCAAG G UCUGCAU	1741	AUGCAAGA GCcgaagGCGaGuCaaGGuCu CUUGGGCA	9312
1679	GACUUUCA G CAAUGUCA	1742	UGACAUUG GCcgaagGCGaGuCaaGGuCu UGAAAGUC	9313
1703	ACCUUGAG G CAUACUUC	1743	GAAGUAUG GCcgaagGCGaGuCaaGGuCu CUCAAGGU	9314
1732	UUUAAUGA G UGGGAGGA	1744	UCCUCCCA GCcgaagGCGaGuCaaGGuCu UCAUUAAA	9315
1741	UGGGAGGA G UUGGGGA	1745	UCCCCCAA GCcgaagGCGaGuCaaGGuCu UCCUCCCA	9316
1754	GGGAGGAG G UUAGGUUA	1746	UAACCUAA GCcgaagGCGaGuCaaGGuCu CUCCUCCC	9317
1759	GAGGUUAG G UUAAGGU	1747	ACCUUUA GCcgaagGCGaGuCaaGGuCu CUAACCUC	9318
1766	GGUUAAG G UCUUUGUA	1748	UACAAAGA GCcgaagGCGaGuCaaGGuCu CUUUAACC	9319
1782	ACUAGGAG G CUGUAGGC	1749	GCCUACAG GCcgaagGCGaGuCaaGGuCu CUCCUAGU	9320
1789	GGCUGUAG G CAUAAAUU	1750	AAUUUAUG GCcgaagGCGaGuCaaGGuCu CUACAGCC	9321
1799	AUAAAUUG G UGUGUUA	1751	UGAACACA GCcgaagGCGaGuCaaGGuCu CAAUUUAU	9322
1811	GUUCACCA G CACCAUGC	1752	GCAUGGUG GCcgaagGCGaGuCaaGGuCu UGGUGAAC	9323
1870	CUGUUCAA G CCUCCAAG	1753	CUUGGAGG GCcgaagGCGaGuCaaGGuCu UUGAACAG	9324
1878	GCCUCCAA G CUGUGCCU	1754	AGGCACAG GCcgaagGCGaGuCaaGGuCu UUGGAGGC	9325
1890	UGCCUUGG G UGGCUUUG	1755	CAAAGCCA GCcgaagGCGaGuCaaGGuCu CCAAGGCA	9326
1893	CUUGGGUG G CUUUGGGG	1756	CCCCAAAG GCcgaagGCGaGuCaaGGuCu CACCCAAG	9327
1901	GCUUUGGG G CAUGGACA	1757	UGUCCAUG GCcgaagGCGaGuCaaGGuCu CCCAAAGC	9328
1917	AUUGACCC G UAUAAAGA	1758	UCUUUAUA GCcgaagGCGaGuCaaGGuCu GGGUCAAU	9329
1933	AAUUUGGA G CUUCUGUG	1759	CACAGAAG GCcgaagGCGaGuCaaGGuCu UCCAAAUU	9330
1944	UCUGUGGA G UUACUCUC	1760	GAGAGUAA GCcgaagGCGaGuCaaGGuCu UCCACAGA	9331
2023	AUCGGGGG G CCUAGAG	1761	CUCUAAGG GCcgaagGCGaGuCaaGGuCu CCCCAGAU	9332
2031	GCCUUAAGA G UCUCCGGA	1762	UCCGGAGA GCcgaagGCGaGuCaaGGuCu UCUAAGGC	9333
2062	ACCAUACG G CACUCAGG	1763	CCUGAGUG GCcgaagGCGaGuCaaGGuCu CGUAUGGU	9334
2070	GCACUCAG G CAAGCUAU	1764	AUAGCUUG GCcgaagGCGaGuCaaGGuCu CUGAGUGC	9335
2074	UCAGGCAA G CUAUUCUG	1765	CAGAAUAG GCcgaagGCGaGuCaaGGuCu UUGCCUGA	9336
2090	GUGUUGGG G UGAGUUGA	1766	UCAACUCA GCcgaagGCGaGuCaaGGuCu CCCAACAC	9337
2094	UGGGGUGA G UUGAUGAA	1767	UUCAUCA GCcgaagGCGaGuCaaGGuCu UCACCCA	9338
2107	UGAAUCUA G CCACCUGG	1768	CCAGUGGG GCcgaagGCGaGuCaaGGuCu UAGAUUCA	9339
2116	CCACCUGG G UGGGAAGU	1769	ACUUCCTA GCcgaagGCGaGuCaaGGuCu CCAGUGG	9340
2123	GGUGGGAA G UAAUUGG	1770	CCAAAUUA GCcgaagGCGaGuCaaGGuCu UUCCACC	9341
2140	AAGAUGCA G CAUCCAGG	1771	CCUGGAUG GCcgaagGCGaGuCaaGGuCu UGGAUCUU	9342
2155	GGGAAUUA G UAGUCAGC	1772	GCUGACUA GCcgaagGCGaGuCaaGGuCu UAAUUCCT	9343
2158	AAUUAGUA G UCAGCUAU	1773	AUAGCUGA GCcgaagGCGaGuCaaGGuCu UACUAAUU	9344
2162	AGUAGUCA G CUAUGUCA	1774	UGACAUAG GCcgaagGCGaGuCaaGGuCu UGACUACU	9345
2173	AUGUCAAC G UUAUAUUG	1775	CAUAUUUA GCcgaagGCGaGuCaaGGuCu GUUGACAU	9346
2183	UAAUAUGG G CCUAAAAA	1776	UUUUUAGG GCcgaagGCGaGuCaaGGuCu CCAUAUUA	9347
2208	CUAUUGUG G UUUCACAU	1777	AUGUGAAA GCcgaagGCGaGuCaaGGuCu CACAAUAG	9348
2235	ACUUUUGG G CGAGAAAC	1778	GUUUCUCG GCcgaagGCGaGuCaaGGuCu CCAAAAGU	9349
2260	AAUAUUUG G UGUCUUUU	1779	AAAAGACA GCcgaagGCGaGuCaaGGuCu CAAAUUUU	9350
2272	CUUUUGGA G UGUGGAUU	1780	AAUCCACA GCcgaagGCGaGuCaaGGuCu UCCAAAAG	9351
2360	ACGAAGAG G CAGGUCCC	1781	GGGACCUG GCcgaagGCGaGuCaaGGuCu CUCUUCGU	9352
2364	AGAGGCAG G UCCCCUAG	1782	CUAGGGGA GCcgaagGCGaGuCaaGGuCu CUGCCUCU	9353
2403	AGACGAAG G UCUCAAUC	1783	GAUUGAGA GCcgaagGCGaGuCaaGGuCu CUUCGUCU	9354
2417	AUCGCCGC G UCGCAGAA	1784	UUCUGCGA GCcgaagGCGaGuCaaGGuCu GCGGCGAU	9355
2454	CAAUUUUA G UAUUCCUU	1785	AAGGAUA GCcgaagGCGaGuCaaGGuCu UAACAUG	9356
2474	CACAUAA G UGGGAAAC	1786	GUUUCCCA GCcgaagGCGaGuCaaGGuCu CUUAUGUG	9357

2491	UUUACGGG G CUUUAUUC	1787	GAAUAAAG GCcgaagGCGaGuCaaGGuCu	CCCUGAAA	9358
2507	CUUCUACG G UACCUUGC	1788	GCAAGGUA GCcgaagGCGaGuCaaGGuCu	CGUAGAAG	9359
2530	CCUAAAUG G CAAACUCC	1789	GGAGUUUG GCcgaagGCGaGuCaaGGuCu	CAUUUAGG	9360
2587	AGAUGUAA G CAUUUUGU	1790	ACAAAUUG GCcgaagGCGaGuCaaGGuCu	UUACAUCU	9361
2599	UUUGUGGG G CCCCUUAC	1791	GUAAGGGG GCcgaagGCGaGuCaaGGuCu	CCCACAAA	9362
2609	CCCUUACA G UAAAUUGA	1792	UUCAUUUA GCcgaagGCGaGuCaaGGuCu	UGUAAGGG	9363
2650	CCUGCUAG G UUUUAUCC	1793	GGAUAAAA GCcgaagGCGaGuCaaGGuCu	CUAGCAGG	9364
2701	AUCAAACC G UAUUAUCC	1794	GGAUAAUA GCcgaagGCGaGuCaaGGuCu	GGUUUGAU	9365
2713	UAUCCAGA G UAUGUAGU	1795	ACUACAUA GCcgaagGCGaGuCaaGGuCu	UCUGGAUA	9366
2720	AGUAUGUA G UAAUCAU	1796	AUGAUUAA GCcgaagGCGaGuCaaGGuCu	UACAUAUCU	9367
2768	UUUGGAAG G CGGGGAUC	1797	GAUCCCCG GCcgaagGCGaGuCaaGGuCu	CUUCCAAA	9368
2791	AAAAGAGA G UCCACACG	1798	CGUGUGGA GCcgaagGCGaGuCaaGGuCu	UCUCUUUU	9369
2799	GUCCACAC G UAGCGCCU	1799	AGGCGCUA GCcgaagGCGaGuCaaGGuCu	GUGUGGAC	9370
2802	CACACGUA G CGCCUCAU	1800	AUGAGGCG GCcgaagGCGaGuCaaGGuCu	UACGUGUG	9371
2818	UUUUGCGG G UCACCAUA	1801	UAUGGUGA GCcgaagGCGaGuCaaGGuCu	CCGCAAAA	9372
2848	GAUCUACA G CAUGGGAG	1802	CUCCCAUG GCcgaagGCGaGuCaaGGuCu	UGUAGAUC	9373
2857	CAUGGGAG G UUGGUCUU	1803	AAGACCAA GCcgaagGCGaGuCaaGGuCu	CUCCCAUG	9374
2861	GGAGGUUG G UCUUCCAA	1804	UUGGAAGA GCcgaagGCGaGuCaaGGuCu	CAACCUCC	9375
2881	UCGAAAAG G CAUGGGGA	1805	UCCCCAUG GCcgaagGCGaGuCaaGGuCu	CUUUUCGA	9376
2936	GAUCAUCA G UUGGACCC	1806	GGGUCCAA GCcgaagGCGaGuCaaGGuCu	UGAUGAUC	9377
2955	CAUUCAAA G CCAACUCA	1807	UGAGUUGG GCcgaagGCGaGuCaaGGuCu	UUUGAAUG	9378
2964	CCAACUCA G UAAAUCCA	1808	UGGAUUUA GCcgaagGCGaGuCaaGGuCu	UGAGUUGG	9379
3005	GACAACUG G CCGACGCG	1809	GCGUCCGG GCcgaagGCGaGuCaaGGuCu	CAGUUGUC	9380
3021	CCAACAAG G UGGGAGUG	1810	CACUCCCA GCcgaagGCGaGuCaaGGuCu	CUUGUUGG	9381
3027	AGGUGGGA G UGGGAGCA	1811	UGCUCCCA GCcgaagGCGaGuCaaGGuCu	UCCACCCU	9382
3033	GAGUGGGA G CAUUCGGG	1812	CCCGAAUG GCcgaagGCGaGuCaaGGuCu	UCCACUC	9383
3041	GCAUUCGG G CCAGGGUU	1813	AACCCUGG GCcgaagGCGaGuCaaGGuCu	CCGAAUGC	9384
3047	GGGCCAGG G UUCACCCC	1814	GGGGUGAA GCcgaagGCGaGuCaaGGuCu	CCUGGCCC	9385
3077	CUGUUGGG G UGGAGCCC	1815	GGGCUCCA GCcgaagGCGaGuCaaGGuCu	CCCAACAG	9386
3082	GGGUGGA G CCCUCACG	1816	CGUGAGGG GCcgaagGCGaGuCaaGGuCu	UCCACCCC	9387
3097	CGCUCAGG G CCUACUCA	1817	UGAGUAGG GCcgaagGCGaGuCaaGGuCu	CCUGAGCG	9388
3117	CUGUGCCA G CAGCUCCU	1818	AGGAGCUG GCcgaagGCGaGuCaaGGuCu	UGGCACAG	9389
3120	UGCCAGCA G CUCCUCCU	1819	AGGAGGAG GCcgaagGCGaGuCaaGGuCu	UGCUGGCA	9390
3146	ACCAAUCG G CAGUCAGG	1820	CCUGACUG GCcgaagGCGaGuCaaGGuCu	CGAUUGGU	9391
3149	AAUCGGCA G UCAGGAAG	1821	CUUCCUGA GCcgaagGCGaGuCaaGGuCu	UGCCGAUU	9392
3158	UCAGGAAG G CAGCCUAC	1822	GUAGGCUG GCcgaagGCGaGuCaaGGuCu	CUUCCUGA	9393
3161	GGAAGGCA G CCUACUCC	1823	GGAGUAGG GCcgaagGCGaGuCaaGGuCu	UGCCUUC	9394
3204	AUCCUCAG G CCAUGCAG	1824	CUGCAUGG GCcgaagGCGaGuCaaGGuCu	CUGAGGAU	9395

Input Sequence = AF100308. Cut Site = YG/M or UG/U.

Stem Length = 8 . Core Sequence = GCcgaagGCGaGuCaaGGuCu

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

TABLE IX: HUMAN HBV DNAZYME AND SUBSTRATE SEQUENCE

Pos	Substrate	Seq ID	DNAzyme	Seq ID
508	CAACCAGC A CCGGACCA	833	TGGTCCGG GGCTAGCTACAACGA GCTGGTTG	9396
1632	GAACGCC A CAGGAACC	1096	GGTTCCTG GGCTAGCTACAACGA GGGCGTTC	9397
2992	CAACCCGC A CAAGGACA	1376	TGTCCCTG GGCTAGCTACAACGA GCGGGTTG	9398
61	ACUUUCCU G CUGGUGGC	1448	GCCACCAG GGCTAGCTACAACGA AGGAAAGT	9399
94	UGAGCCCU G CUCAGAAU	1450	ATTCTGAG GGCTAGCTACAACGA AGGGCTCA	9400
112	CUGUCUCU G CCAUAUCG	1451	CGATATGG GGCTAGCTACAACGA AGAGACAG	9401
169	AGAACAUC G CAUCAGGA	1454	TCCTGATG GGCTAGCTACAACGA GATGTTCT	9402
192	GGACCCCU G CUCGUGUU	1455	AACACGAG GGCTAGCTACAACGA AGGGGTCC	9403
315	CAAAAUUC G CAGUCCCA	1457	TGGGACTG GGCTAGCTACAACGA GAATTTTG	9404
374	UGGUUAUC G CUGGAUGU	1458	ACATCCAG GGCTAGCTACAACGA GATAACCA	9405
387	AUGUGUCU G CGGCGUUU	1459	AAACGCCG GGCTAGCTACAACGA AGACACAT	9406
410	CUUCCUCU G CAUCCUGC	1460	GCAGGATG GGCTAGCTACAACGA AGAGGAAG	9407
417	UGCAUCCU G CUGCUAUG	1461	CATAGCAG GGCTAGCTACAACGA AGGATGCA	9408
420	AUCCUGCU G CUAUGCCU	1462	AGGCATAG GGCTAGCTACAACGA AGCAGGAT	9409
425	GCUGCUAU G CCUCAUCU	1463	AGATGAGG GGCTAGCTACAACGA ATAGCAGC	9410
468	GGUAUGUU G CCCGUUUG	1464	CAAACGGG GGCTAGCTACAACGA AACATACC	9411
518	CGGACCAU G CAAAACCU	1465	AGGTTTTC GGCTAGCTACAACGA ATGGTCCG	9412
527	CAAAACCU G CACAACUC	1466	GAGTTGTG GGCTAGCTACAACGA AGGTTTTC	9413
538	CAACUCCU G CUCAAGGA	1467	TCCTTGAG GGCTAGCTACAACGA AGGAGTTG	9414
569	CUCAUGUU G CUGUACAA	1468	TTGTACAG GGCTAGCTACAACGA AACATGAG	9415
596	CGGAAACU G CACCUGUA	1469	TACAGGTG GGCTAGCTACAACGA AGTTTCCG	9416
631	GGGCUUUC G CAAAUAAC	1470	GTATTTTC GGCTAGCTACAACGA GAAAGCCC	9417
687	UUACUAGU G CCAUUUGU	1471	ACAAATGG GGCTAGCTACAACGA ACTAGTAA	9418
795	CCCUUUAU G CCGCUGUU	1474	AACAGCGG GGCTAGCTACAACGA ATAAAGGG	9419
798	UUUAUGCC G CUGUUACC	1475	GGTAACAG GGCTAGCTACAACGA GGCATAAA	9420
911	GGCACAUC G CCACAGGA	1476	TCCTGTGG GGCTAGCTACAACGA AATGTGCC	9421
1020	UGGGGUUU G CCGCCCCU	1479	AGGGGCGG GGCTAGCTACAACGA AAACCCCA	9422
1023	GGUUUGCC G CCCCUUUC	1480	GAAAGGGG GGCTAGCTACAACGA GGCAAACC	9423
1034	CCUUUCAC G CAUUGUGG	1481	CCACATTG GGCTAGCTACAACGA GTGAAAGG	9424
1050	GAUAUUCU G CUUUAUUA	1482	CATTAAAG GGCTAGCTACAACGA AGAATATC	9425
1058	GCUUUAU G CCUUUAUA	1483	TATAAAGG GGCTAGCTACAACGA ATTAAAGC	9426
1068	CUUUAUUA G CAUGCAUA	1484	TATGCATG GGCTAGCTACAACGA ATATAAAG	9427
1072	AUAUGCAU G CAUACAAG	1485	CTGTATG GGCTAGCTACAACGA ATGCATAT	9428
1103	ACUUUCUC G CCAACUUA	1486	TAAGTTGG GGCTAGCTACAACGA GAGAAAGT	9429
1155	ACCCCGUU G CUCGGCAA	1488	TTGCCGAG GGCTAGCTACAACGA AACGGGGT	9430
1177	UGGUCUAU G CCAAGUGU	1489	ACACTTGG GGCTAGCTACAACGA ATAGACCA	9431
1188	AAGUGUUU G CUGACGCA	1490	TGCGTCAG GGCTAGCTACAACGA AAACACTT	9432
1194	UUGCUGAC G CAACCCCC	1492	GGGGGTTG GGCTAGCTACAACGA GTCAGCAA	9433
1234	CCAUCAGC G CAUGCGUG	1493	CACGCATG GGCTAGCTACAACGA GCTGATGG	9434
1238	CAGCGCAU G CGUGGAAC	1494	GTTCCACG GGCTAGCTACAACGA ATGCGCTG	9435
1262	UCUCCUCU G CCGAUCCA	1495	TGGATCGG GGCTAGCTACAACGA AGAGGAGA	9436
1275	UCCAUAAC G CGGAACUC	1497	GAGTTCCG GGCTAGCTACAACGA GGTATGGA	9437
1290	UCCUAGCC G CUUGUUUU	1498	AAAACAAG GGCTAGCTACAACGA GGCTAGGA	9438
1299	CUUGUUUU G CUCGCAGC	1499	GCTGCGAG GGCTAGCTACAACGA AAAACAAG	9439
1303	UUUUGCUC G CAGCAGGU	1500	ACCTGCTG GGCTAGCTACAACGA GAGCAAAA	9440
1349	UCUGUCGU G CUCUCCCG	1502	CGGGAGAG GGCTAGCTACAACGA ACGACAGA	9441
1357	GCUCUCCC G CAAUAUA	1503	TATATTTG GGCTAGCTACAACGA GGGAGAGC	9442

1382	CCAUGGCU G CUAGGCUG	1504	CAGCCTAG GGCTAGCTACAACGA AGCCATGG	9443
1392	UAGGCUGU G CUGCCAAC	1505	GTTGGCAG GGCTAGCTACAACGA ACAGCCTA	9444
1395	GCUGUGCU G CCAACUGG	1506	CCAGTTGG GGCTAGCTACAACGA AGCACAGC	9445
1411	GAUCCUAC G CGGGACGU	1507	ACGTCCCG GGCTAGCTACAACGA GTAGGATC	9446
1442	CCGUCGGC G CUGAAUCC	1508	GGATTCTAG GGCTAGCTACAACGA GCCGACGG	9447
1452	UGAAUCCC G CGGACGAC	1510	GTCGTCCG GGCTAGCTACAACGA GGGATTCA	9448
1474	CCGGGGCC G CUUGGGGC	1512	GCCCCAAG GGCTAGCTACAACGA GGCCCCGG	9449
1489	GCUCUACC G CCCGCUUC	1513	GAAGCGGG GGCTAGCTACAACGA GGTAGAGC	9450
1493	UACCGCCC G CUUCUCCG	1514	CGGAGAAG GGCTAGCTACAACGA GGGCGGTA	9451
1501	GCUUCUCC G CCUAUUGU	1515	ACAATAGG GGCTAGCTACAACGA GGAGAAGC	9452
1528	CACGGGGC G CACCUCUC	1517	GAGAGGTG GGCTAGCTACAACGA GCCCCGTG	9453
1542	CUCUUUAC G CGGACUCC	1518	GGAGTCCG GGCTAGCTACAACGA GTAAAGAG	9454
1559	CCGUCUGU G CCUUCUCA	1519	TGAGAAGG GGCTAGCTACAACGA ACAGACGG	9455
1571	UCUCAUCU G CCGGACCG	1520	CGGTCCGG GGCTAGCTACAACGA AGATGAGA	9456
1583	GACCGUGU G CACUUCGC	1521	GCGAAGTG GGCTAGCTACAACGA ACACGGTC	9457
1590	UGCACUUC G CUUCACCU	1522	AGGTGAAG GGCTAGCTACAACGA GAAGTGCA	9458
1601	UCACCUCU G CACGUCGC	1523	GCGACGTG GGCTAGCTACAACGA AGAGGTGA	9459
1608	UGCACGUC G CAUGGAGA	1524	TCTCCATG GGCTAGCTACAACGA GACGTGCA	9460
1628	CCGUGAAC G CCCACAGG	1526	CCTGTGGG GGCTAGCTACAACGA GTTCACGG	9461
1642	AGGAACCU G CCCAAGGU	1527	ACCTTGGG GGCTAGCTACAACGA AGGTTCTT	9462
1654	AAGGUCUU G CAUAAGAG	1528	CTCTTATG GGCTAGCTACAACGA AAGACCTT	9463
1818	AGCACCAU G CAACUUUU	1533	AAAAGTTG GGCTAGCTACAACGA ATGGTGCT	9464
1835	UCACCUCU G CCUAAUCA	1534	TGATTAGG GGCTAGCTACAACGA AGAGGTGA	9465
1883	CAAGCUGU G CCUUGGGU	1535	ACCCAAGG GGCTAGCTACAACGA ACAGCTTG	9466
1959	UCUUUUUU G CCUUCUGA	1537	TCAGAAGG GGCTAGCTACAACGA AAAAAAGA	9467
2002	UCGACACC G CCUCUGCU	1541	AGCAGAGG GGCTAGCTACAACGA GGTGTCGA	9468
2008	CCGCCUCU G CUCUGUAU	1542	ATACAGAG GGCTAGCTACAACGA AGAGGCGG	9469
2282	GUGGAUUC G CACUCCUC	1548	GAGGAGTG GGCTAGCTACAACGA GAATCCAC	9470
2293	CUCUCCU G CAUAUAGA	1549	TCTATATG GGCTAGCTACAACGA AGGAGGAG	9471
2311	CACCAAAU G CCCUAUC	1550	GATAGGGG GGCTAGCTACAACGA ATTTGGTG	9472
2388	ACUCCCUC G CCUCGCAG	1552	CTGCGAGG GGCTAGCTACAACGA GAGGGAGT	9473
2393	CUCGCCUC G CAGACGAA	1553	TTCGTCTG GGCTAGCTACAACGA GAGGCGAG	9474
2412	UCUCAAUC G CCGCGUCG	1555	CGACGCGG GGCTAGCTACAACGA GATTGAGA	9475
2415	CAAUCGCC G CGUCGCAG	1556	CTGCGACG GGCTAGCTACAACGA GGCATTG	9476
2420	GCCGCGUC G CAGAAGAU	1557	ATCTTCTG GGCTAGCTACAACGA GACGCGGC	9477
2514	GGUACCUU G CUUUAUUC	1558	GATTAAAG GGCTAGCTACAACGA AAGGTACC	9478
2560	AUUCAUUU G CAGGAGGA	1560	TCCTCCTG GGCTAGCTACAACGA AAATGAAT	9479
2641	UUAACUUA G CCUGCUAG	1563	CTAGCAGG GGCTAGCTACAACGA ATAGTTAA	9480
2645	CUAUGCCU G CUAGGUUU	1564	AAACCTAG GGCTAGCTACAACGA AGGCATAG	9481
2677	AAAUUUUU G CCCUUAGA	1565	TCTAAGGG GGCTAGCTACAACGA AAATATTT	9482
2740	UUCACGAC G CGACAUUA	1566	TAATGTCTG GGCTAGCTACAACGA GTCTGGAA	9483
2804	CACGUAGC G CCUCAUUU	1568	AAATGAGG GGCTAGCTACAACGA GCTACGTG	9484
2814	CUCAUUUU G CGGGUCAC	1569	GTGACCCG GGCTAGCTACAACGA AAAATGAG	9485
2946	UGGACCCU G CAUUCAAA	1572	TTTGAATG GGCTAGCTACAACGA AGGGTCCA	9486
2990	CUCAACCC G CACAAGGA	1573	TCCTTGTG GGCTAGCTACAACGA GGGTTGAG	9487
3012	GGCCGGAC G CCAACAAG	1574	CTTGTGTG GGCTAGCTACAACGA GTCCGGCC	9488
3090	GCCCUCAC G CUCAGGGC	1575	GCCCTGAG GGCTAGCTACAACGA GTGAGGGC	9489
3113	ACAACUGU G CCAGCAGC	1576	GCTGCTGG GGCTAGCTACAACGA ACAGTTGT	9490
3132	CUCCUCCU G CCUCCACC	1577	GGTGGAGG GGCTAGCTACAACGA AGGAGGAG	9491
51	AGGGCCCU G UACUUUCC	1578	GGAAAGTA GGCTAGCTACAACGA AGGGCCCT	9492
106	AGAAUACU G UCUCUGCC	1579	GGCAGAGA GGCTAGCTACAACGA AGTATTCT	9493

148	GGGACCCU G UACCGAAC	1580	GTTCGGTA GGCTAGCTACAACGA AGGGTCCC	9494
198	CUGCUCGU G UUACAGGC	1581	GCCTGTAA GGCTAGCTACAACGA ACGAGCAG	9495
219	UUUUUCUU G UUGACAAA	1582	TTTGTCAA GGCTAGCTACAACGA AAGAAAAA	9496
297	ACACCCGU G UGUCUUGG	1583	CCAAGACA GGCTAGCTACAACGA ACGGGTGT	9497
299	ACCCGUGU G UCUUGGCC	1584	GGCCAAGA GGCTAGCTACAACGA ACACGGGT	9498
347	ACCAACCU G UUGUCCUC	1585	GAGGACAA GGCTAGCTACAACGA AGGTGTGT	9499
350	AACCUGUU G UCCUCCAA	1586	TTGGAGGA GGCTAGCTACAACGA AACAGGTT	9500
362	UCCAAUUU G UCCUGGUU	1587	AACCAGGA GGCTAGCTACAACGA AAATTGGA	9501
381	CGCUGGAU G UGUCUGCG	1588	CGCAGACA GGCTAGCTACAACGA ATCCAGCG	9502
383	CUGGAUGU G UUGCGGC	1589	GCCGCAGA GGCTAGCTACAACGA ACATCCAG	9503
438	AUCUUCUU G UUGUUCU	1590	AGAACCAA GGCTAGCTACAACGA AAGAAGAT	9504
465	CAAGGUAU G UUGCCCGU	1591	ACGGGCAA GGCTAGCTACAACGA ATACCTTG	9505
476	GCCCGUUU G UCCUCUAA	1592	TTAGAGGA GGCTAGCTACAACGA AAACGGGC	9506
555	ACCUCUAU G UUUCCUC	1593	GAGGGAAA GGCTAGCTACAACGA ATAGAGGT	9507
566	UCCCUCAU G UUGCUGUA	1594	TACAGCAA GGCTAGCTACAACGA ATGAGGGA	9508
572	AUGUUGCU G UACAAAAC	1595	GT'TTTGTA GGCTAGCTACAACGA AGCAACAT	9509
602	CUGCACCU G UAUUCCCA	1596	TGGGAATA GGCTAGCTACAACGA AGGTGCAG	9510
694	UGCAUUU G UUCAGUGG	1597	CCACTGAA GGCTAGCTACAACGA AAATGGCA	9511
724	CCCCACU G UCGGCCUU	1598	AAGCCAGA GGCTAGCTACAACGA AGTGGGGG	9512
750	UGGAUGAU G UGGUUUUG	1599	CAAACCA GGCTAGCTACAACGA ATCATCCA	9513
771	CCAAGUCU G UACAACAU	1600	ATGTTGTA GGCTAGCTACAACGA AGACTTGG	9514
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818	UUUCUUU G UCUUGGG	1602	CCCAAGA GGCTAGCTACAACGA AAAAGAAA	9516
888	UGGGAUUAU G UAAUUGGG	1603	CCCAATTA GGCTAGCTACAACGA ATATCCCA	9517
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944	AUCAAAU G UGUUUUAG	1605	CTAAACA GGCTAGCTACAACGA ATTTTGAT	9519
946	CAAAUGU G UUUUAGGA	1606	TCCTAAAA GGCTAGCTACAACGA ACATTTTG	9520
963	AACUCCU G UAAACAGG	1607	CCTGTTTA GGCTAGCTACAACGA AGGAAGTT	9521
991	GAAAGUAU G UCAACGAA	1608	TTCGTTGA GGCTAGCTACAACGA ATACTTTC	9522
1002	AACGAAU G UGGGUCUU	1609	AAGACCCA GGCTAGCTACAACGA AATTCGTT	9523
1039	CACGAAU G UGGAUUAU	1610	AATATCCA GGCTAGCTACAACGA ATTGCGTG	9524
1137	AACAGUAU G UGAACCUU	1611	AAGGTTCA GGCTAGCTACAACGA ATACTGTT	9525
1184	UGCAAGU G UUUGCUGA	1612	TCAGAAA GGCTAGCTACAACGA ACTTGGCA	9526
1251	GAACUUU G UGUCUCCU	1613	AGGAGACA GGCTAGCTACAACGA AAAGGTTT	9527
1253	ACCUUUGU G UCUCUCU	1614	AGAGGAGA GGCTAGCTACAACGA ACAAAGGT	9528
1294	AGCCGCUU G UUUUGCUC	1615	GAGCAAAA GGCTAGCTACAACGA AAGCGGCT	9529
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1390	GCUAGGCU G UGCUGCCA	1617	TGGCAGCA GGCTAGCTACAACGA AGCCTAGC	9531
1425	CGUCCUUU G UUUACGUC	1618	GACGTAAA GGCTAGCTACAACGA AAAGGACG	9532
1508	CGCCUAU G UACCGACC	1619	GGTCGGTA GGCTAGCTACAACGA AATAGGCG	9533
1557	CCCCGUCU G UGCCUUCU	1620	AGAAGGCA GGCTAGCTACAACGA AGACGGGG	9534
1581	CGGACCGU G UGCACUUC	1621	GAAGTGCA GGCTAGCTACAACGA ACGGTCCG	9535
1684	UCAGCAU G UCAACGAC	1622	GTCGTTGA GGCTAGCTACAACGA ATTGCTGA	9536
1719	CAAAGACU G UGUGUUUA	1623	TAAACACA GGCTAGCTACAACGA AGTCTTTG	9537
1721	AAGACUGU G UGUUUAAU	1624	ATTAAACA GGCTAGCTACAACGA ACAGTCTT	9538
1723	GACUGUGU G UUUAAUGA	1625	TCATTAAA GGCTAGCTACAACGA ACACAGTC	9539
1772	AGGUCUUU G UACUAGGA	1626	TCCTAGTA GGCTAGCTACAACGA AAAGACCT	9540
1785	AGGAGGCU G UAGGCAUA	1627	TATGCCTA GGCTAGCTACAACGA AGCTCCT	9541
1801	AAAUUGGU G UGUUCACC	1628	GGTGAACA GGCTAGCTACAACGA ACCAATTT	9542
1803	AUUGGUGU G UUCACCAG	1629	CTGGTGAA GGCTAGCTACAACGA ACACCAAT	9543
1850	CAUCUCAU G UUCAUGUC	1630	GACATGAA GGCTAGCTACAACGA ATGAGATG	9544

1856	AUGUUCAU G UCCUACUG	1631	CAGTAGGA GGCTAGCTACAACGA ATGAACAT	9545
1864	GUCCUACU G UUCAAGCC	1632	GGCTTGAA GGCTAGCTACAACGA AGTAGGAC	9546
1881	UCCAAGCU G UGCCUUGG	1633	CCAAGGCA GGCTAGCTACAACGA AGCTTGGA	9547
1939	GAGCUUCU G UGGAGUUA	1634	TAACTCCA GGCTAGCTACAACGA AGAAGCTC	9548
2013	UCUGCUCU G UAUCGGGG	1635	CCCCGATA GGCTAGCTACAACGA AGAGCAGA	9549
2045	GGAACAUU G UUCACCUC	1636	GAGGTGAA GGCTAGCTACAACGA AATGTTCC	9550
2082	GCUAUUCU G UGUUGGGG	1637	CCCCAACA GGCTAGCTACAACGA AGAATAGC	9551
2084	UAUUCUGU G UUGGGGUG	1638	CACCCCAA GGCTAGCTACAACGA ACAGAATA	9552
2167	UCAGCUAU G UCAACGUU	1639	AACGTTGA GGCTAGCTACAACGA ATAGCTGA	9553
2205	CAACUAUU G UGGUUUCA	1640	TGAAACCA GGCTAGCTACAACGA AATAGTTG	9554
2222	CAUUUCCU G UCUUACUU	1641	AAGTAAGA GGCTAGCTACAACGA AGGAAATG	9555
2245	GAGAAACU G UUCUUGAA	1642	TTCAAGAA GGCTAGCTACAACGA AGTTTCTC	9556
2262	UAUUUGGU G UCUUUUGG	1643	CCAAAAGA GGCTAGCTACAACGA ACCAAATA	9557
2274	UUUGGAGU G UGGAUUCG	1644	CGAATCCA GGCTAGCTACAACGA ACTCCAAA	9558
2344	AAACUACU G UUGUUAGA	1645	TCTAACAA GGCTAGCTACAACGA AGTAGTTT	9559
2347	CUACUGUU G UUAGACGA	1646	TCGTCTAA GGCTAGCTACAACGA AACAGTAG	9560
2450	AUCUCAAU G UUAGUAUU	1647	AATACTAA GGCTAGCTACAACGA ATTGAGAT	9561
2573	AGGACAUU G UUGAUAGA	1648	TCTATCAA GGCTAGCTACAACGA AATGTCCT	9562
2583	UGAUAGAU G UAAGCAAU	1649	ATTGCTTA GGCTAGCTACAACGA ATCTATCA	9563
2594	AGCAAUUU G UGGGGCCC	1650	GGGCCCCA GGCTAGCTACAACGA AAATTGCT	9564
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3071	GGGGGACU G UUGGGGUG	1654	CACCCCAA GGCTAGCTACAACGA AGTCCCCC	9568
3111	UCACAACU G UGCCAGCA	1655	TGCTGGCA GGCTAGCTACAACGA AGTTGTGA	9569
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46	GAGUCAGG G CCCUGUAC	1657	GTACAGGG GGCTAGCTACAACGA CCTGACTC	9571
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85	CAGGAACA G UGAGCCCU	1661	AGGGCTCA GGCTAGCTACAACGA TGTTCTCTG	9575
89	AACAGUGA G CCCUGCUC	1662	GAGCAGGG GGCTAGCTACAACGA TCACTGTT	9576
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205	UGUUACAG G CGGGGUUU	1665	AAACCCCG GGCTAGCTACAACGA CTGTAACA	9579
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248	ACCACAGA G UCUAGACU	1667	AGTCTAGA GGCTAGCTACAACGA TCTGTGGT	9581
258	CUAGACUC G UGGUGGAC	1668	GTCCACCA GGCTAGCTACAACGA GAGTCTAG	9582
261	GACUCGUG G UGGACUUC	1669	GAAGTCCA GGCTAGCTACAACGA CACGAGTC	9583
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305	GUGUCUUG G CCAAAAUU	1671	AATTTTGG GGCTAGCTACAACGA CAAGACAC	9585
318	AAUUCGCA G UCCCCAAU	1672	ATTTGGGA GGCTAGCTACAACGA TGCGAATT	9586
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658	GGGCCUCA G UCCGUUUC	1684	GAAACGGA GGCTAGCTACAACGA TGAGGCCC	9598
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767	GGGGCCAA G UCUGUACA	1697	TGTACAGA GGCTAGCTACAACGA TTGGCCCC	9611
785	CAUCUUGA G UCCCUUUA	1698	TAAAGGGA GGCTAGCTACAACGA TCAAGATG	9612
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1225	GGCCAUAG G CCAUCAGC	1719	GCTGATGG GGCTAGCTACAACGA CTATGGCC	9633
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1347	AUUCUGUC G UGCUCUCC	1726	GGAGAGCA GGCTAGCTACAACGA GACAGAAT	9640
1379	UUUCCAUG G CUGCUAGG	1727	CCTAGCAG GGCTAGCTACAACGA CATGGAAA	9641
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1418	CGCGGGAC G UCCUUUGU	1729	ACAAAGGA GGCTAGCTACAACGA GTCCCGCG	9643
1431	UUGUUUAC G UCCCGUCG	1730	CGACGGGA GGCTAGCTACAACGA GTAAACAA	9644
1436	UACGUCCC G UCGGCGCU	1731	AGCGCCGA GGCTAGCTACAACGA GGGACGTA	9645
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1517	UACCGACC G UCCACGGG	1735	CCCCTGGA GGCTAGCTACAACGA GGTCGGTA	9649
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1553	GACUCCCC G UCUGUGCC	1737	GGCACAGA GGCTAGCTACAACGA GGGGAGTC	9651
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1605	CUCUGCAC G UCGAUGG	1739	CCATGCGA GGCTAGCTACAACGA GTGCAGAG	9653
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1741	UGGGAGGA G UUGGGGGA	1745	TCCCCCAA GGCTAGCTACAACGA TCCTCCCA	9659
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1766	GGUUAAG G UCUUGUA	1748	TACAAAGA GGCTAGCTACAACGA CTTTAACC	9662
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1917	AUUGACCC G UAUAAAGA	1758	TCTTTATA GGCTAGCTACAACGA GGGTCAAT	9672
1933	AAUUUGGA G CUUCUGUG	1759	CACAGAAG GGCTAGCTACAACGA TCCAAATT	9673
1944	UCUGUGGA G UUACUCUC	1760	GAGAGTAA GGCTAGCTACAACGA TCCACAGA	9674
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2031	GCCUUAGA G UCUCCGGA	1762	TCCGGAGA GGCTAGCTACAACGA TCTAAGGC	9676
2062	ACCAUACG G CACUCAGG	1763	CCTGAGTG GGCTAGCTACAACGA CGTATGGT	9677
2070	GCACUCAG G CAAGCUAU	1764	ATAGCTTG GGCTAGCTACAACGA CTGAGTGC	9678
2074	UCAGGCAA G CUAUUCUG	1765	CAGAATAG GGCTAGCTACAACGA TTGCTGTA	9679
2090	GUGUUGGG G UGAGUUGA	1766	TCAACTCA GGCTAGCTACAACGA CCCAACAC	9680
2094	UGGGGUGA G UUGAUGAA	1767	TTCATCAA GGCTAGCTACAACGA TCACCCCA	9681
2107	UGAAUCUA G CCACCUGG	1768	CCAGGTGG GGCTAGCTACAACGA TAGATTCA	9682
2116	CCACCUGG G UGGGAAGU	1769	ACTTCCCA GGCTAGCTACAACGA CCAGGTGG	9683
2123	GGUGGGAA G UAAUUUGG	1770	CCAAATTA GGCTAGCTACAACGA TTCCCACC	9684
2140	AAGAUGCA G CAUCCAGG	1771	CCTGGATG GGCTAGCTACAACGA TGGATCTT	9685
2155	GGGAAUUA G UAGUCAGC	1772	GCTGACTA GGCTAGCTACAACGA TAATTCCC	9686
2158	AAUUAGUA G UCAGCUAU	1773	ATAGCTGA GGCTAGCTACAACGA TACTAATT	9687
2162	AGUAGUCA G CUAUGUCA	1774	TGACATAG GGCTAGCTACAACGA TGACTACT	9688
2173	AUGUCAAC G UUAUAUG	1775	CATATTAA GGCTAGCTACAACGA GTTGACAT	9689
2183	UAAUAUGG G CCUAAAAA	1776	TTTTTAGG GGCTAGCTACAACGA CCAATTA	9690
2208	CUAUUGUG G UUCACAU	1777	ATGTGAAA GGCTAGCTACAACGA CACAATAG	9691
2235	ACUUUUGG G CGAGAAAC	1778	GTTTCTCG GGCTAGCTACAACGA CCAAAAGT	9692
2260	AAUAUUUG G UGUCUUUU	1779	AAAAGACA GGCTAGCTACAACGA CAAATATT	9693
2272	CUUUUGGA G UGUGGAUU	1780	AATCCACA GGCTAGCTACAACGA TCCAAAAG	9694
2360	ACGAAGAG G CAGGUCCC	1781	GGGACCTG GGCTAGCTACAACGA CTCTTCGT	9695
2364	AGAGGCAG G UCCCCUAG	1782	CTAGGGGA GGCTAGCTACAACGA CTGCCTCT	9696
2403	AGACGAAG G UCUCAAUC	1783	GATTGAGA GGCTAGCTACAACGA CTTCGTCT	9697

2417	AUCGCCGC G UCGCAGAA	1784	TTCTGCGA GGCTAGCTACAACGA GCGGCGAT	9698
2454	CAAUGUUA G UAUUCCUU	1785	AAGGAATA GGCTAGCTACAACGA TAACATTG	9699
2474	CACAUAA G UGGGAAAC	1786	GTTTCCCA GGCTAGCTACAACGA CTTATGTG	9700
2491	UUUACGGG G CUUUAUUC	1787	GAATAAAG GGCTAGCTACAACGA CCCGTAAG	9701
2507	CUUCUACG G UACCUUGC	1788	GCAAGGTA GGCTAGCTACAACGA CGTAGAAG	9702
2530	CCUAAAUG G CAAACUCC	1789	GGAGTTTG GGCTAGCTACAACGA CATTTAGG	9703
2587	AGAUGUAA G CAAUUUGU	1790	ACAAATTG GGCTAGCTACAACGA TTACATCT	9704
2599	UUUGUGGG G CCCCUIAC	1791	GTAAGGGG GGCTAGCTACAACGA CCCACAAA	9705
2609	CCCUUACA G UAAAUGAA	1792	TTCATTTA GGCTAGCTACAACGA TGTAAGGG	9706
2650	CCUGCUAG G UUUUAUCC	1793	GGATAAAA GGCTAGCTACAACGA CTAGCAGG	9707
2701	AUCAAAAC G UAUUAUCC	1794	GGATAATA GGCTAGCTACAACGA GGTTTGAT	9708
2713	UAUCCAGA G UAUGUAGU	1795	ACTACATA GGCTAGCTACAACGA TCTGGATA	9709
2720	AGUAUGUA G UAAAUCAU	1796	ATGATTAA GGCTAGCTACAACGA TACATACT	9710
2768	UUUGGAAG G CGGGGAUC	1797	GATCCCCG GGCTAGCTACAACGA CTTCCAAA	9711
2791	AAAAGAGA G UCCACACG	1798	CGTGTGGA GGCTAGCTACAACGA TCTCTTTT	9712
2799	GUCCACAC G UAGCGCCU	1799	AGGCGCTA GGCTAGCTACAACGA GTGTGGAC	9713
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2818	UUUUGCGG G UCACCAUA	1801	TATGGTGA GGCTAGCTACAACGA CCGCAAAA	9715
2848	GAUCUACA G CAUGGGAG	1802	CTCCCATG GGCTAGCTACAACGA TGTAAGTC	9716
2857	CAUGGGAG G UUGGUCUU	1803	AAGACCAA GGCTAGCTACAACGA CTCCCATG	9717
2861	GGAGGUUG G UCUUCCAA	1804	TTGGAAGA GGCTAGCTACAACGA CAACCTCC	9718
2881	UCGAAAAG G CAUGGGGA	1805	TCCCCATG GGCTAGCTACAACGA CTTTTCGA	9719
2936	GAUCAUCA G UUGGACCC	1806	GGGTCCAA GGCTAGCTACAACGA TGATGATC	9720
2955	CAUUCAAA G CCAACUCA	1807	TGAGTTGG GGCTAGCTACAACGA TTTGAATG	9721
2964	CCAACUCA G UAAAUCCA	1808	TGGATTGA GGCTAGCTACAACGA TGAGTTGG	9722
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3021	CCAACAAG G UGGGAGUG	1810	CACTCCCA GGCTAGCTACAACGA CTTGTTGG	9724
3027	AGGUGGGA G UGGGAGCA	1811	TGCTCCCA GGCTAGCTACAACGA TCCCACCT	9725
3033	GAGUGGGA G CAUUCGGG	1812	CCCGAATG GGCTAGCTACAACGA TCCCCTC	9726
3041	GCAUUCGG G CCAGGUU	1813	AACCTGGG GGCTAGCTACAACGA CCGAATGC	9727
3047	GGGCCAGG G UUCACCCC	1814	GGGGTGAA GGCTAGCTACAACGA CTGAGCCC	9728
3077	CUGUUGGG G UGGAGCCC	1815	GGGCTCCA GGCTAGCTACAACGA CCAACAG	9729
3082	GGGGUGGA G CCCUCACG	1816	CGTGAGGG GGCTAGCTACAACGA TCCACCCC	9730
3097	CGCUCAGG G CCUACUCA	1817	TGAGTAGG GGCTAGCTACAACGA CCTGAGCG	9731
3117	CUGUGCCA G CAGCUCCU	1818	AGGAGCTG GGCTAGCTACAACGA TGGCACAG	9732
3120	UGCCAGCA G CUCCUCCU	1819	AGGAGGAG GGCTAGCTACAACGA TGCTGGCA	9733
3146	ACCAAUUG G CAGUCAGG	1820	CCTGACTG GGCTAGCTACAACGA CGATTGGT	9734
3149	AAUCGGCA G UCAGGAAG	1821	CTTCCTGA GGCTAGCTACAACGA TGCCGATT	9735
3158	UCAGGAAG G CAGCCUAC	1822	GTAGGCTG GGCTAGCTACAACGA CTTCTCTG	9736
3161	GGAAGGCA G CCUACUCC	1823	GGAGTAGG GGCTAGCTACAACGA TGCTTCC	9737
3204	AUCCUCAG G CCAUGCAG	1824	CTGCATGG GGCTAGCTACAACGA CTGAGGAT	9738
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17	CACUUUCC A CCAAACUC	706	GAGTTTGG GGCTAGCTACAACGA GGAAAGTG	9740
22	UCCACCAA A CUCUCAA	1825	TTGAAGAG GGCTAGCTACAACGA TTGGTGGA	9741
32	UCUUCAAG A UCCCAGAG	1826	CTCTGGGA GGCTAGCTACAACGA CTTGAAGA	9742
53	GGCCCUGU A CUUCCUG	42	CAGGAAAG GGCTAGCTACAACGA ACAGGGCC	9743
82	GUUCAGGA A CAGUGAGC	1827	GCTCACTG GGCTAGCTACAACGA TCCTGAAC	9744
101	UGCUCAGA A UACUGUCU	1828	AGACAGTA GGCTAGCTACAACGA TCTGAGCA	9745
103	CUCAGAAU A CUGUCUCU	50	AGAGACAG GGCTAGCTACAACGA ATTCTGAG	9746
115	UCUCUGCC A UAUUGUCA	737	TGACGATA GGCTAGCTACAACGA GGCAGAGA	9747
117	UCUGCCAU A UCGUCAAU	53	ATTGACGA GGCTAGCTACAACGA ATGGCAGA	9748

124	UAUCGUCA A UCUUAUCG	1829	CGATAAGA GGCTAGCTACAACGA TGACGATA	9749
129	UCAAUCUU A UCGAAGAC	58	GTCTTCGA GGCTAGCTACAACGA AAGATTGA	9750
136	UAUCGAAG A CUGGGGAC	1830	GTCCCCAG GGCTAGCTACAACGA CTTTCGATA	9751
143	GACUGGGG A CCCUGUAC	1831	GTACAGGG GGCTAGCTACAACGA CCCCAGTC	9752
150	GACCCUGU A CCGAACAU	60	ATGTTCCG GGCTAGCTACAACGA ACAGGGTC	9753
155	UGUACCGA A CAUGGAGA	1832	TCTCCATG GGCTAGCTACAACGA TCGGTACA	9754
157	UACCGAAC A UGGAGAAC	745	GTTCTCCA GGCTAGCTACAACGA GTTCGGTA	9755
164	CAUGGAGA A CAUCGAU	1833	ATGCGATG GGCTAGCTACAACGA TCTCCATG	9756
166	UGGAGAAC A UCGCAUCA	746	TGATGCGA GGCTAGCTACAACGA GTTCTCCA	9757
171	AACAUCGC A UCAGGACU	747	AGTCCTGA GGCTAGCTACAACGA GCGATGTT	9758
177	GCAUCAGG A CUCCUAGG	1834	CCTAGGAG GGCTAGCTACAACGA CCTGATGC	9759
186	CUCCUAGG A CCCUGCU	1835	AGCAGGGG GGCTAGCTACAACGA CCGAGGAG	9760
201	CUCGUGUU A CAGGCGGG	67	CCCCTCTG GGCTAGCTACAACGA AACACGAG	9761
223	UCUUGUUG A CAAAAAUC	1836	GATTTTTG GGCTAGCTACAACGA CAACAAGA	9762
229	UGACAAAA A UCCUCACA	1837	TGTGAGGA GGCTAGCTACAACGA TTTTGTCA	9763
235	AAAUCCUC A CAAUACCA	762	TGGTATTG GGCTAGCTACAACGA GAGGATT	9764
238	UCCUCACA A UACCACAG	1838	CTGTGGTA GGCTAGCTACAACGA TGTGAGGA	9765
240	CUCACAAU A CCACAGAG	77	CTCTGTGG GGCTAGCTACAACGA ATTGTGAG	9766
243	ACAAUACC A CAGAGUCU	765	AGACTCTG GGCTAGCTACAACGA GGTATTGT	9767
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265	CGUGGUGG A CUUCUCUC	1840	GAGAGAAG GGCTAGCTACAACGA CCACCACG	9769
275	UUCUCUCA A UUUUCUAG	1841	CTAGAAAA GGCTAGCTACAACGA TGAGAGAA	9770
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291	GGGGGAAC A CCCGUGUG	774	CACACGGG GGCTAGCTACAACGA GTTCCCCC	9772
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379	AUCGCUGG A UGUGUCUG	1847	CAGACACA GGCTAGCTACAACGA CCAGGAT	9780
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412	UCCUCUGC A UCCUGCUG	807	CAGCAGGA GGCTAGCTACAACGA GCAGAGGA	9783
423	CUGCUGCU A UGCCUCAU	119	ATGAGGCA GGCTAGCTACAACGA AGCAGCAG	9784
430	UAUGCCUC A UCUUCUUG	814	CAAGAAGA GGCTAGCTACAACGA GAGGCATA	9785
452	UCUUCUGG A CUAUCAAG	1848	CTTGATAG GGCTAGCTACAACGA CCAGAAGA	9786
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1409	UGGAUCCU A CGCGGGAC	332	GTCCCGCG GGCTAGCTACAACGA AGGATCCA	9902
1416	UACGCGGG A CGUCCUUU	1900	AAAGGACG GGCTAGCTACAACGA CCCGCGTA	9903
1429	CUUUGUUU A CGUCCCGU	338	ACGGGACG GGCTAGCTACAACGA AAACAAAG	9904
1447	GGCGCUGA A UCCCGCGG	1901	CCGCGGGA GGCTAGCTACAACGA TCAGCGCC	9905
1456	UCCCGCGG A CGACCCCU	1902	AGGGGTCG GGCTAGCTACAACGA CCGCGGGA	9906
1459	CGCGGACG A CCCCUCUC	1903	GGGAGGGG GGCTAGCTACAACGA CGTCCGCG	9907
1486	GGGGCUCU A CCGCCCGC	345	GCGGGCGG GGCTAGCTACAACGA AGAGCCCC	9908
1505	CUCCGCCU A UUGUACCG	349	CGGTACAA GGCTAGCTACAACGA AGGCGGAG	9909
1510	CCUAUUGU A CCGACCGU	351	ACGGTCCG GGCTAGCTACAACGA ACAATAGG	9910
1514	UUGUACCG A CCGUCCAC	1904	GTGGACGG GGCTAGCTACAACGA CCGTACAA	9911
1521	GACCGUCC A CGGGGCGC	1064	GCGCCCCG GGCTAGCTACAACGA GGACGGTC	9912
1530	CGGGGCGC A CCUCUCUU	1065	AAGAGAGG GGCTAGCTACAACGA GCGCCCCG	9913
1540	CUCUCUUU A CGCGGACU	357	AGTCCGCG GGCTAGCTACAACGA AAAGAGAG	9914
1546	UUACGCGG A CUCCCCGU	1905	ACGGGGAG GGCTAGCTACAACGA CCGCGTAA	9915
1567	GCCUUCUC A UCUGCCGG	1078	CCGGCAGA GGCTAGCTACAACGA GAGAAGGC	9916
1576	UCUGCCGG A CCGUGUGC	1906	GCACACGG GGCTAGCTACAACGA CCGGCAGA	9917
1585	CCGUGUGC A CUUCGCUU	1082	AAGCGAAG GGCTAGCTACAACGA GCACACGG	9918
1595	UUCGCUUC A CCUCUGCA	1085	TGCAGAGG GGCTAGCTACAACGA GAAGCGAA	9919
1603	ACCUCUGC A CGUCGAU	1089	ATGCGACG GGCTAGCTACAACGA GCAGAGGT	9920
1610	CACGUCGC A UGGAGACC	1090	GGTCTCCA GGCTAGCTACAACGA GCGACGTG	9921
1616	GCAUGGAG A CCACCGUG	1907	CACGGTGG GGCTAGCTACAACGA CTCCATGC	9922
1619	UGGAGACC A CCGUGAAC	1092	GTTACCGG GGCTAGCTACAACGA GGTCTCCA	9923
1626	CACCGUGA A CGCCACAA	1908	TGTGGGCG GGCTAGCTACAACGA TCACGGTG	9924
1638	CCACAGGA A CCUGCCCA	1909	TGGGCAGG GGCTAGCTACAACGA TCCTGTGG	9925
1656	GGUCUUGC A UAAGAGGA	1104	TCCTCTTA GGCTAGCTACAACGA GCAAGACC	9926
1664	AUAAGAGG A CUCUUGGA	1910	TCCAAGAG GGCTAGCTACAACGA CCTCTTAT	9927
1672	ACUCUUGG A CUUUCAGC	1911	GCTGAAAG GGCTAGCTACAACGA CCAAGAGT	9928
1682	UUUCAGCA A UGUCAACG	1912	CGTTGACA GGCTAGCTACAACGA TGCTGAAA	9929
1688	CAAUGUCA A CGACCGAC	1913	GTGCGTCG GGCTAGCTACAACGA TGACATTG	9930
1691	UGUCAACG A CCGACCUU	1914	AAGGTCCG GGCTAGCTACAACGA CGTTGACA	9931
1695	AACGACCG A CCUUGAGG	1915	CCTCAAGG GGCTAGCTACAACGA CGGTCGTT	9932
1705	CUUGAGGC A UACUUCAA	1114	TTGAAGTA GGCTAGCTACAACGA GCCTCAAG	9933
1707	UGAGGCAU A CUUCAAAG	380	CTTTGAAG GGCTAGCTACAACGA ATGCCTCA	9934
1716	CUUCAAAG A CUGUGUGU	1916	ACACACAG GGCTAGCTACAACGA CTTTGAAG	9935
1728	UGUGUUUA A UGAGUGGG	1917	CCCACTCA GGCTAGCTACAACGA TAAACACA	9936
1774	GUCUUUGU A CUAGGAGG	394	CCTCCTAG GGCTAGCTACAACGA ACAAAGAC	9937
1791	CUGUAGGC A UAAAUUGG	1121	CCAATTTA GGCTAGCTACAACGA GCCTACAG	9938
1795	AGGCAUAA A UUGGUGUG	1918	CACACCAA GGCTAGCTACAACGA TTATGCCT	9939
1807	GUGUGUUC A CCAGCACC	1122	GGTGCTGG GGCTAGCTACAACGA GAACACAC	9940
1813	UCACCAGC A CCAUGCAA	1125	TTGCATGG GGCTAGCTACAACGA GCTGGTGA	9941
1816	CCAGCACC A UGCAACUU	1127	AAGTTGCA GGCTAGCTACAACGA GGTGCTGG	9942
1821	ACCAUGCA A CUUUUUCA	1919	TGAAAAAG GGCTAGCTACAACGA TGCATGGT	9943
1829	ACUUUUUC A CCUCUGCC	1130	GGCAGAGG GGCTAGCTACAACGA GAAAAAGT	9944
1840	UCUGCCUA A UCAUCUCA	1920	TGAGATGA GGCTAGCTACAACGA TAGGCAGA	9945
1843	GCCUAAUC A UCUCUUGU	1136	ACATGAGA GGCTAGCTACAACGA GATTAGGC	9946
1848	AUCAUCUC A UGUUCAUG	1138	CATGAACA GGCTAGCTACAACGA GAGATGAT	9947
1854	UCAUGUUC A UGUCCUAC	1139	GTAGGACA GGCTAGCTACAACGA GAACATGA	9948
1861	CAUGUCCU A CUGUUCAA	414	TTGAACAG GGCTAGCTACAACGA AGGACATG	9949
1903	UUUGGGGC A UGGACAUU	1152	AATGTCCA GGCTAGCTACAACGA GCCCCAAA	9950
1907	GGGCAUGG A CAUUGACC	1921	GGTCAATG GGCTAGCTACAACGA CCATGCCC	9951
1909	GCAUGGAC A UUGACCCG	1153	CGGGTCAA GGCTAGCTACAACGA GTCCATGC	9952

1913	GGACAUUG A CCCGUAAU	1922	TATACGGG GGCTAGCTACAACGA CAATGTCC	9953
1919	UGACCCGU A UAAAGAAU	422	ATTCTTTA GGCTAGCTACAACGA ACGGGTCA	9954
1926	UAUAAAGA A UUUGGAGC	1923	GCTCCAAA GGCTAGCTACAACGA TCTTTATA	9955
1947	GUGGAGUU A CUCUCUUU	429	AAAGAGAG GGCTAGCTACAACGA AACTCCAC	9956
1967	GCCUUCUG A CUUCUUUC	1924	GAAAGAAG GGCTAGCTACAACGA CAGAAGGC	9957
1981	UUCUUCU A UUCGAGAU	446	ATCTCGAA GGCTAGCTACAACGA AGAAGGAA	9958
1988	UAUUCGAG A UCUCUCG	1925	CGAGGAGA GGCTAGCTACAACGA CTCGAATA	9959
1997	UCUCCUCG A CACCGCCU	1926	AGGCGGTG GGCTAGCTACAACGA CGAGGAGA	9960
1999	UCCUCGAC A CCGCCUCU	1172	AGAGGCGG GGCTAGCTACAACGA GTCGAGGA	9961
2015	UGCUCUGU A UCGGGGGG	454	CCCCCGA GGCTAGCTACAACGA ACAGAGCA	9962
2040	UCUCCGGA A CAUUGUUC	1927	GAACAATG GGCTAGCTACAACGA TCCGGAGA	9963
2042	UCCGGAAC A UUGUUCAC	1183	GTGAACAA GGCTAGCTACAACGA GTTCCGGA	9964
2049	CAUUGUUC A CCUCACCA	1184	TGGTGAGG GGCTAGCTACAACGA GAACAATG	9965
2054	UUCACCUC A CCAUACGG	1187	CCGTATGG GGCTAGCTACAACGA GAGGTGAA	9966
2057	ACCUCACC A UACGGCAC	1189	GTGCCGTA GGCTAGCTACAACGA GGTGAGGT	9967
2059	CUCACCAU A CGGCACUC	464	GAGTGCCG GGCTAGCTACAACGA ATGGTGAG	9968
2064	CAUACGGC A CUCAGGCA	1190	TGCCTGAG GGCTAGCTACAACGA GCCGTATG	9969
2077	GGCAAGCU A UUCUGUGU	466	ACACAGAA GGCTAGCTACAACGA AGCTTGCC	9970
2098	GUGAGUUG A UGAAUCUA	1928	TAGATTCA GGCTAGCTACAACGA CAACTCAC	9971
2102	GUUGAUGA A UCUAGCCA	1929	TGGCTAGA GGCTAGCTACAACGA TCATCAAC	9972
2110	AUCUAGCC A CCUGGGUG	1198	CACCCAGG GGCTAGCTACAACGA GGCTAGAT	9973
2126	GGGAAGUA A UUUGGAAG	1930	CTTCCAAA GGCTAGCTACAACGA TACTTCCC	9974
2135	UUUGGAAG A UCCAGCAU	1931	ATGCTGGA GGCTAGCTACAACGA CTTCCAAA	9975
2142	GAUCCAGC A UCCAGGGA	1203	TCCCTGGA GGCTAGCTACAACGA GCTGGATC	9976
2151	UCCAGGGA A UUAGUAGU	1932	ACTACTAA GGCTAGCTACAACGA TCCCTGGA	9977
2165	AGUCAGCU A UGUCAACG	482	CGTTGACA GGCTAGCTACAACGA AGCTGACT	9978
2171	CUAUGUCA A CGUAAUA	1933	TATTAACG GGCTAGCTACAACGA TGACATAG	9979
2177	CAACGUUA A UAUGGGCC	1934	GGCCCAT A GGCTAGCTACAACGA TAACGTTG	9980
2179	ACGUUAAU A UGGGCCUA	486	TAGGCCCC GGCTAGCTACAACGA ATTAACGT	9981
2191	GCCUAAAA A UGAGACAA	1935	TTGTCTGA GGCTAGCTACAACGA TTTTAGGC	9982
2196	AAAAUCAG A CAACUAUU	1936	AATAGTTG GGCTAGCTACAACGA CTGATTTT	9983
2199	AUCAGACA A CUAUUGUG	1937	CACAATAG GGCTAGCTACAACGA TGTCTGAT	9984
2202	AGACAACU A UUGUGGUU	489	AACCACAA GGCTAGCTACAACGA AGTTGTCT	9985
2213	GUGGUUUC A CAUUUCCU	1214	AGGAAATG GGCTAGCTACAACGA GAAACCAC	9986
2215	GGUUUCAC A UUUCUGU	1215	ACAGGAAA GGCTAGCTACAACGA GTGAAACC	9987
2227	CCUGUCUU A CUUUUGGG	499	CCCAAAAG GGCTAGCTACAACGA AAGACAGG	9988
2242	GGCGAGAA A CUGUUCUU	1938	AAGAACAG GGCTAGCTACAACGA TTCTCGCC	9989
2253	GUUCUUGA A UAUUUGGU	1939	ACCAAATA GGCTAGCTACAACGA TCAAGAAC	9990
2255	UCUUGAAU A UUUGGUGU	506	ACACCAAA GGCTAGCTACAACGA ATTCAAGA	9991
2278	GAGUGUGG A UUCGCACU	1940	AGTGCGAA GGCTAGCTACAACGA CCACACTC	9992
2284	GGAUUCGC A CUCCUCCU	1223	AGGAGGAG GGCTAGCTACAACGA GCGAATCC	9993
2295	CCUCCUGC A UAUAGACC	1229	GGTCTATA GGCTAGCTACAACGA GCAGGAGG	9994
2297	UCCUGCAU A UAGACCAC	517	GTGGTCTA GGCTAGCTACAACGA ATGCAGGA	9995
2301	GCAUAUAG A CCACCAAA	1941	TTTGGTGG GGCTAGCTACAACGA CTATATGC	9996
2304	UAUAGACC A CCAA AUGC	1231	GCATTTGG GGCTAGCTACAACGA GGTCTATA	9997
2309	ACCACCAA A UGCCCCUA	1942	TAGGGGCA GGCTAGCTACAACGA TTGGTGGT	9998
2317	AUGCCCCU A UCUAUCA	519	TGATAAGA GGCTAGCTACAACGA AGGGGCAT	9999
2322	CCUAUCUU A UCAACACU	522	AGTGTTGA GGCTAGCTACAACGA AAGATAGG	10000
2326	UCUAUCA A CACUCCG	1943	CGGAAGTG GGCTAGCTACAACGA TGATAAGA	10001
2328	UUAUCAAC A CUUCCGGA	1240	TCCGGAAG GGCTAGCTACAACGA GTTGATAA	10002
2338	UUCCGGAA A CUACUGUU	1944	AACAGTAG GGCTAGCTACAACGA TTCCGGAA	10003

2341	CGGAAACU A CUGUUGUU	526	AACAACAG GGCTAGCTACAACGA AGTTTCCG	10004
2352	GUUGUUAG A CGAAGAGG	1945	CCTCTTCG GGCTAGCTACAACGA CTAACAAC	10005
2380	GAAGAAGA A CUCCUCUG	1946	CGAGGGAG GGCTAGCTACAACGA TCTTCTTC	10006
2397	CCUCGCAG A CGAAGGUC	1947	GACCTTCG GGCTAGCTACAACGA CTGCGAGG	10007
2409	AGGUCUCA A UCGCCGCG	1948	CGCGGCGA GGCTAGCTACAACGA TGAGACCT	10008
2427	CGCAGAAG A UCUCAAUC	1949	GATTGAGA GGCTAGCTACAACGA CTTCTGCG	10009
2433	AGAUCUCA A UCUCGGGA	1950	TCCCGAGA GGCTAGCTACAACGA TGAGATCT	10010
2442	UCUCGGGA A UCUCAAUG	1951	CATTGAGA GGCTAGCTACAACGA TCCCGAGA	10011
2448	GAAUCUCA A UGUUAGUA	1952	TACTAACA GGCTAGCTACAACGA TGAGATTC	10012
2456	AUGUUAGU A UUCUUGG	547	CCAAGGAA GGCTAGCTACAACGA ACTAACAT	10013
2465	UUCUUGG A CACAUAA	1953	CTTATGTG GGCTAGCTACAACGA CCAAGGAA	10014
2467	CCUUGGAC A CAUAAGGU	1268	ACCTTATG GGCTAGCTACAACGA GTCCAAGG	10015
2469	UUGGACAC A UAAGGUGG	1269	CCACCTTA GGCTAGCTACAACGA GTGTCCAA	10016
2481	GGUGGGAA A CUUUACGG	1954	CCGTAAAG GGCTAGCTACAACGA TTCCCACC	10017
2486	GAAACUUU A CGGGGCUU	554	AAGCCCCG GGCTAGCTACAACGA AAAGTTTC	10018
2496	GGGGCUUU A UUCUUCUA	557	TAGAAGAA GGCTAGCTACAACGA AAAGCCCC	10019
2504	AUUCUUCU A CGGUACCU	562	AGGTACCG GGCTAGCTACAACGA AGAAGAAT	10020
2509	UCUACGGU A CCUUGCUU	563	AAGCAAGG GGCTAGCTACAACGA ACCGTAGA	10021
2520	UUGCUUUA A UCCUAAAU	1955	ATTTAGGA GGCTAGCTACAACGA TAAAGCAA	10022
2527	AAUCCUAA A UGGCAAAC	1956	GTTTGCCA GGCTAGCTACAACGA TTAGGATT	10023
2534	AAUGGCAA A CUCCUUCU	1957	AGAAGGAG GGCTAGCTACAACGA TTGCCATT	10024
2550	UUUCCUG A CAUUCUU	1958	AATGAATG GGCTAGCTACAACGA CAGGAAAA	10025
2552	UUCUGAC A UUCAUUUG	1286	CAATGAA GGCTAGCTACAACGA GTCAGGAA	10026
2556	UGACAUUC A UUUGCAGG	1287	CCTGCAAA GGCTAGCTACAACGA GAATGTCA	10027
2568	GCAGGAGG A CAUUGUUG	1959	CAACAATG GGCTAGCTACAACGA CCTCCTGC	10028
2570	AGGAGGAC A UUGUUGAU	1289	ATCAACAA GGCTAGCTACAACGA GTCCTCCT	10029
2577	CAUUGUUG A UAGAUGUA	1960	TACATCTA GGCTAGCTACAACGA CAACAATG	10030
2581	GUUGAUAG A UGUAAGCA	1961	TGCTTACA GGCTAGCTACAACGA CTATCAAC	10031
2590	UGUAAGCA A UUUGUGGG	1962	CCCACAAA GGCTAGCTACAACGA TGCTTACA	10032
2606	GGCCCCUU A CAGUAAAU	588	ATTTACTG GGCTAGCTACAACGA AAGGGGCC	10033
2613	UACAGUAA A UGAAAACA	1963	TGTTTCA GGCTAGCTACAACGA TTACTGTA	10034
2619	AAAUGAAA A CAGGAGAC	1964	GTCTCCTG GGCTAGCTACAACGA TTTTATT	10035
2626	AACAGGAG A CUUAAAUU	1965	AATTTAAG GGCTAGCTACAACGA CTCCTGTT	10036
2632	AGACUUAA A UUAACUUA	1966	ATAGTTAA GGCTAGCTACAACGA TTAAGTCT	10037
2636	UUAAAUAU A CUAUGCCU	1967	AGGCATAG GGCTAGCTACAACGA TAATTTAA	10038
2639	AAUUAACU A UGCCUGCU	594	AGCAGGCA GGCTAGCTACAACGA AGTTAATT	10039
2655	UAGGUUUU A UCCCAAUG	599	CATTGGGA GGCTAGCTACAACGA AAAACCTA	10040
2661	UUAUCCCA A UGUUACUA	1968	TAGTAACA GGCTAGCTACAACGA TGGGATAA	10041
2666	CCAAUGUU A CUAAUAU	602	ATATTTAG GGCTAGCTACAACGA AACATTGG	10042
2671	GUUACUAA A UAUUUGCC	1969	GGCAAATA GGCTAGCTACAACGA TTAGTAAC	10043
2673	UACUAAAU A UUUGCCCU	604	AGGGCAAA GGCTAGCTACAACGA ATTTAGTA	10044
2685	GCCCUUAG A UAAAGGGA	1970	TCCCTTTA GGCTAGCTACAACGA CTAAGGGC	10045
2693	AUAAAGGG A UCAAACCG	1971	CGGTTTGA GGCTAGCTACAACGA CCCTTTAT	10046
2698	GGGAUCAA A CCGUAUUA	1972	TAATACGG GGCTAGCTACAACGA TTGATCCC	10047
2703	CAAACCGU A UUAUCCAG	611	CTGGATAA GGCTAGCTACAACGA ACGGTTTG	10048
2706	ACCGUAUU A UCCAGAGU	613	ACTCTGGA GGCTAGCTACAACGA AATACGGT	10049
2715	UCCAGAGU A UGUAGUUA	615	TAATAACA GGCTAGCTACAACGA ACTCTGGA	10050
2724	UGUAGUUA A UCAUUACU	1973	AGTAATGA GGCTAGCTACAACGA TAACTACA	10051
2727	AGUUAUUC A UUUAUCC	1313	GGAAGTAA GGCTAGCTACAACGA GATTAACT	10052
2730	UAAUCAUU A CUUCCAGA	621	TCTGGAAG GGCTAGCTACAACGA AATGATTA	10053
2738	ACUUCAG A CGCGACAU	1974	ATGTCGCG GGCTAGCTACAACGA CTGGAAGT	10054

2743	CAGACGCG A CAUUAUUU	1975	AAATAATG GGCTAGCTACAACGA CGCGTCTG	10055
2745	GACGCGAC A UUAUUUAC	1317	GTAAATAA GGCTAGCTACAACGA GTCGCGTC	10056
2748	GCGACAUU A UUUACACA	625	TGTGTAAA GGCTAGCTACAACGA AATGTCGC	10057
2752	CAUUAUUU A CACACUCU	628	AGAGTGTG GGCTAGCTACAACGA AAATAATG	10058
2754	UUAUUUAC A CACUCUUU	1318	AAAGAGTG GGCTAGCTACAACGA GTAAATAA	10059
2756	AUUUACAC A CUCUUUGG	1319	CCAAAGAG GGCTAGCTACAACGA GTGTAAAT	10060
2774	AGGCGGGG A UCUUAUUAU	1976	ATATAAGA GGCTAGCTACAACGA CCCC GCCT	10061
2779	GGGAUCUU A UAUAAAAG	634	CTTTTATA GGCTAGCTACAACGA AAGATCCC	10062
2781	GAUCUUUAU A UAAAAGAG	635	CTCTTTTA GGCTAGCTACAACGA ATAAGATC	10063
2795	GAGAGUCC A CAGUAGC	1324	GCTACGTG GGCTAGCTACAACGA GGAATCTC	10064
2797	GAGUCCAC A CGUAGCGC	1325	GCGCTACG GGCTAGCTACAACGA GTGGACTC	10065
2809	AGCGCCUC A UUUUGCGG	1328	CCGCAAAA GGCTAGCTACAACGA GAGGCGCT	10066
2821	UGCGGGUC A CCAUAUUC	1329	GAATAATG GGCTAGCTACAACGA GACCCGCA	10067
2824	GGGUCACC A UAUCUUG	1331	CAAGAATA GGCTAGCTACAACGA GGTGACCC	10068
2826	GUCACCAU A UUCUUGGG	644	CCCAAGAA GGCTAGCTACAACGA ATGGTGAC	10069
2836	UCUUGGGA A CAAGAUCU	1977	AGATCTTG GGCTAGCTACAACGA TCCCAAGA	10070
2841	GGAACAAG A UCUACAGC	1978	GCTGTAGA GGCTAGCTACAACGA CTTGTTCC	10071
2845	CAAGAUCU A CAGCAUGG	649	CCATGCTG GGCTAGCTACAACGA AGATCTTG	10072
2850	UCUACAGC A UGGGAGGU	1336	ACCTCCCA GGCTAGCTACAACGA GCTGTAGA	10073
2870	UCUCCAA A CCUCGAAA	1979	TTTCGAGG GGCTAGCTACAACGA TTGGAAGA	10074
2883	GAAAAGGC A UGGGACA	1342	TGTCCCA GGCTAGCTACAACGA GCCTTTTC	10075
2889	GCAUGGGG A CAAAUUUU	1980	AAGATTTG GGCTAGCTACAACGA CCCCATGC	10076
2893	GGGGACAA A UCUUUCUG	1981	CAGAAAGA GGCTAGCTACAACGA TTGTCCCC	10077
2908	UGUCCCCA A UCCCCUGG	1982	CCAGGGGA GGCTAGCTACAACGA TGGGGACA	10078
2918	CCCCUGGG A UUCUCCCC	1983	GGGAAGAA GGCTAGCTACAACGA CCCAGGGG	10079
2929	CUUCCCCG A UCAUCAGU	1984	ACTGATGA GGCTAGCTACAACGA CGGGGAAG	10080
2932	CCCCGAUC A UCAGUUGG	1358	CCAACTGA GGCTAGCTACAACGA GATCGGGG	10081
2941	UCAGUUGG A CCCUGCAU	1985	ATGCAGGG GGCTAGCTACAACGA CCAACTGA	10082
2948	GACCCUGC A UUCAAGC	1363	GCTTTGAA GGCTAGCTACAACGA GCAGGGTC	10083
2959	CAAAGCCA A CUCAGUAA	1986	TTACTGAG GGCTAGCTACAACGA TGGCTTTG	10084
2968	CUCAGUAA A UCAGAUU	1987	AATCTGGA GGCTAGCTACAACGA TTACTGAG	10085
2974	AAAUCCAG A UUGGGACC	1988	GGTCCCAA GGCTAGCTACAACGA CTGGATTT	10086
2980	AGAUUGGG A CCUCAACC	1989	GGTTGAGG GGCTAGCTACAACGA CCAATCT	10087
2986	GGACCUCA A CCCGCACA	1990	TGTGCGGG GGCTAGCTACAACGA TGAGGTCC	10088
2998	GCACAAGG A CAACUGGC	1991	GCCAGTTG GGCTAGCTACAACGA CTTGTGTC	10089
3001	CAAGGACA A CUGGCCGG	1992	CCGGCCAG GGCTAGCTACAACGA TGTCTTTG	10090
3010	CUGGCCGG A CGCCAACA	1993	TGTTGGCG GGCTAGCTACAACGA CCGGCCAG	10091
3016	GGACGCCA A CAAGGUGG	1994	CCACCTTG GGCTAGCTACAACGA TGGCGTCC	10092
3035	GUGGGAGC A UUCGGGCC	1384	GGCCCGAA GGCTAGCTACAACGA GCTCCAC	10093
3051	CAGGGUUC A CCCUCCCC	1387	GGGAGGGG GGCTAGCTACAACGA GAACCCTG	10094
3061	CCCUCCCC A UGGGGGAC	1395	GTCCCCCA GGCTAGCTACAACGA GGGGAGGG	10095
3068	CAUGGGGG A CUGUUGGG	1995	CCCAACAG GGCTAGCTACAACGA CCCCATG	10096
3088	GAGCCCUC A CGCUCAGG	1400	CCTGAGCG GGCTAGCTACAACGA GAGGGCTC	10097
3101	CAGGGCCU A CUCACAAC	683	GTTGTGAG GGCTAGCTACAACGA AGGCCCTG	10098
3105	GCCUACUC A CAACUGUG	1406	CACAGTTG GGCTAGCTACAACGA GAGTAGGC	10099
3108	UACUCACA A CUGUGCCA	1996	TGGCACAG GGCTAGCTACAACGA TGTGAGTA	10100
3138	CUGCCUCC A CCAAUCGG	1422	CCGATTGG GGCTAGCTACAACGA GGAGGCAG	10101
3142	CUCCACCA A UCGGCAGU	1997	ACTGCCGA GGCTAGCTACAACGA TGGTGGAG	10102
3165	GGCAGCCU A CUCCCUUA	691	TAAGGGAG GGCTAGCTACAACGA AGGCTGCC	10103
3173	ACUCCCUU A UCUCACC	694	GGTGGAGA GGCTAGCTACAACGA AAGGGAGT	10104
3179	UUAUCUCC A CCUCUAAG	1436	CTTAGAGG GGCTAGCTACAACGA GGAGATAA	10105

MBHB02,249-E (400.042US)

3190	UCUAAGGG A CACUCAUC	1998	GATGAGTG GGCTAGCTACAACGA CCCTTAGA	10106
3192	UAAGGGAC A CUCAUCCU	1440	AGGATGAG GGCTAGCTACAACGA GTCCCTTA	10107
3196	GGACACUC A UCCUCAGG	1442	CCTGAGGA GGCTAGCTACAACGA GAGTGTCC	10108
3207	CUCAGGCC A UGCAGUGG	1447	CCACTGCA GGCTAGCTACAACGA GGCCTGAG	10109

Input Sequence = AF100308. Cut Site = YG/M or UG/U.

Stem Length = 8 . Core Sequence = GGCTAGCTACAACGA

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

TABLE X: HUMAN HBV AMBERZYME AND SUBSTRATE SEQUENCE

Pos	Substrate	Seq ID	Amberzyme	Seq ID
61	ACUUUCCU G CUGGUGGC	1448	GCCACCAG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGGAAAAGU	10110
87	GGAACAGU G AGCCCUUGC	1449	GCAGGGCU GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG ACUGUUC	10111
94	UGAGCCU G CUCAGAAU	1450	AUUCUGAG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGGGCUCA	10112
112	CUGUCUCU G CCAUAUCG	1451	CGAUAUGG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGAGACAG	10113
132	AUCUUAUC G AAGACUGG	1452	CCAGUCUU GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG GAUAAGAU	10114
153	CCUGUACC G AACAUUGA	1453	UCCAUGUU GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG GGUACAGG	10115
169	AGAACAU G CAUCAGGA	1454	UCCUGAUG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG GAUGUUCU	10116
192	GGACCCU G CUCGUGUU	1455	AACACGAG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGGGGUCC	10117
222	UUCUUGUU G ACAAUAU	1456	AUUUUGU GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AACAAAGAA	10118
315	CAAAUUC G CAGUCCCA	1457	UGGGACUG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG GAAUUUUG	10119
374	UGGUUAUC G CUGGAUGU	1458	ACAUCGAG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG GAUAACCA	10120
387	AUGUGUCU G CGGCGUUU	1459	AAACGCCG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGACACAU	10121
410	CUUCUCU G CAUCCUGC	1460	GCAGGAUG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGAGGAAG	10122
417	UGCAUCCU G CUGCUAUG	1461	CAUAGCAG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGGAUGCA	10123
420	AUCCUGCU G CUAGCCU	1462	AGGCAUAG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGCAGGAU	10124
425	GCUGCUAU G CCUCAUCU	1463	AGAUGAGG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AUAGCAGC	10125
468	GGUAUGUU G CCCGUUUG	1464	CAAAACGG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AACAUACC	10126
518	CGGACCAU G CAAAACCU	1465	AGGUUUUG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AUGGUCCG	10127
527	CAAAACCU G CACAACUC	1466	GAGUUUGG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGGUUUUG	10128
538	CAACUCCU G CUCAAGGA	1467	UCCUUGAG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGGAGUUG	10129
569	CUCAUGUU G CUGUACAA	1468	UUGUACAG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AACAUAG	10130
596	CGGAAACU G CACCUGUA	1469	UACAGGUG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AGUUUCCG	10131
631	GGGCUUUC G CAAAUAUC	1470	GUUUUUG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG GAAAGCCC	10132
687	UUACUAGU G CCAUUUGU	1471	ACAAUUGG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG ACUAGUAA	10133
747	AUAUGGAU G AUGUGGUU	1472	AACCACAU GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AUCCAUAU	10134
783	AACAUCUU G AGUCCCUU	1473	AAGGACU GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AAGAUGUU	10135
795	CCCUUUUU G CCGCUGUU	1474	AACAGCGG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AUAAAAGG	10136
798	UUUAUGCC G CUGUUUAC	1475	GGUAAACG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG GGCAUAAA	10137
911	GGCACAUU G CCACAGGA	1476	UCCUGUGG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AAUGUGCC	10138
978	GGCCUAUU G AUUGGAAA	1477	UUUCCAAU GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AAUAGGCC	10139
997	AUGUCAAC G AAUUGUGG	1478	CCACAUAU GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG GUUGACAU	10140
1020	UGGGUUU G CCGCCCUU	1479	AGGGCGG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG AAACCCCA	10141
1023	GGUUUGCC G CCCCUUUC	1480	GAAAGGGG GGAGGAAAACUCC CU UCAAGGACAUCGUCGCCGG GGCAAAACC	10142

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1058	GCUUUAU G CCUUUAUA	1483	UAUAAAGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUUAAAGC	10145
1068	CUUUAU G CAUGCAUA	1484	UAUGCAUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUUAUAAAG	10146
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1103	ACUUUCUC G CCAACUUA	1486	UAAGUUGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GAGAAAGU	10148
1139	CAGUAUGU G AACUUUA	1487	UAAAGUUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACAUAUCUG	10149
1155	ACCCGUU G CUCGGCAA	1488	UUGCCGAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AACGGGGU	10150
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1188	AAGUUUU G CUGACGCA	1490	UGCUCAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAACACUU	10152
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1194	UUGCUGAC G CAACCCCC	1492	GGGGUUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GUCAGCAA	10154
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1238	CAGCGCAU G CGUGGAAC	1494	GUUCCAGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUGCGCUG	10156
1262	UCUCCUCU G CCGAUCCA	1495	UGGAUCGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGAGGAGA	10157
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1290	UCCUAGCC G CUUGUUUU	1498	AAACCAAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GGCUAAGGA	10160
1299	CUUGUUUU G CUCGCAGC	1499	GCUGCGAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAAACAAG	10161
1303	UUUUGCUC G CAGCAGGU	1500	ACCUCUGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GAGCAAAA	10162
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1349	UCUGUUGU G CUCUCCCG	1502	CGGGAGAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACGACAGA	10164
1357	GCUCUCCC G CAAUAUA	1503	UAUAUUUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GGGAGAGC	10165
1382	CCAUGGCU G CUAGGCUG	1504	CAGCCUAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGCCAUGG	10166
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1395	GCUGUGCU G CCAACUGG	1506	CCAGUUGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGCACAGC	10168
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1442	CCGUCGGC G CUGAAUCC	1508	GGAUUCAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GCCGACGG	10170
1445	UCGGCGCU G AAUCCCGC	1509	GCGGGAUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGCGCCGA	10171
1452	UGAAUCCC G CGGACGAC	1510	GUCGUCCG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GGGAUUCA	10172
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1489	GCUCUACC G CCGCUUUC	1513	GAAGCGGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GGUAGAGC	10175
1493	UACCGCCC G CUUUCUCC	1514	CGGAGAAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GGGCGGUA	10176
1501	GCUUUCUC G CCUAUUGU	1515	ACAAUAGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GGAGAAGC	10177
1513	AUUGUACC G ACGGUCCA	1516	UGGACGGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GGUACAAU	10178
1528	CACGGGGC G CACCUCUC	1517	GAGAGGUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GCCCGCUG	10179

1542	CUCUUUAC G CGGACUCC	1518	GGAGUCCG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GUAAAGAG	10180
1559	CCGUCUGU G CCUUCUCA	1519	UGAGAAGG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG ACAGACGG	10181
1571	UCUCAUCU G CCGGACCG	1520	CGGUCCGG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGAUGAGA	10182
1583	GACCGUGU G CACUUGCG	1521	GCGAAGUG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG ACACGGUC	10183
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1608	UGCACGUC G CAUGGAGA	1524	UCUCCAUG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GACGUGCA	10186
1624	ACCACCGU G AAGGCCCA	1525	UGGGCGUU GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG ACGGUGGU	10187
1628	CCGUGAAC G CCCACAGG	1526	CCUGUGGG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GUUCACGG	10188
1642	AGGAACCU G CCCAAGGU	1527	ACCUUGGG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGGUTUCCU	10189
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1818	AGCACCAU G CAACUUUU	1533	AAAAGUUG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AUGGUGCU	10195
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1985	UUUAUUC G AGAUCUCC	1539	GGAGAUU GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GAUUGAA	10201
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2237	UUUUGGGC G AGAAACUG	1546	CAGUUUCU GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GCCCAAAA	10208
2251	CUGUUCUU G AAUAUUUG	1547	CAAAUAU GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AAGAACAG	10209
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2293	CUCCUCCU G CAUAUAGA	1549	UCUAUAUG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGGAGGAG	10211
2311	CACCAAAU G CCCUAUC	1550	GAUAGGGG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AUUUGGUG	10212
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2399	UCGCAGAC G AAGGUCUC	1554	GAGACCUU GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GUCUGCGA	10216

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2420	GCCGCGUC G CAGAAGAU	1557	AUCUUCUG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GACGCGGC	10219
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1684	UCAGCAAU G UCAACGAC	1622	GUUGUUGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUUGCUGA	10284
1719	CAAGACU G UGUUUUUA	1623	UAAACACA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGUCUUUG	10285
1721	AAGACUGU G UGUUUAUU	1624	AUUAAAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACAGUCUU	10286
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1772	AGGUUUUU G UACUAGGA	1626	UCCUAGUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAAGACCU	10288
1785	AGGAGGCU G UAGGCAUA	1627	UAUGCCUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGCCUCCU	10289
1801	AAAUUGGU G UGUUCACC	1628	GGUGAACA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACCAAUUU	10290

1803	AUUGGUGU G UUCACCAG	1629	CUGGUGAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG ACACCAAU	10291
1850	CAUCUCAU G UUCAUGUC	1630	GACAUGAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AUGAGAUG	10292
1856	AUGUUCAU G UCCUACUG	1631	CAGUAGGA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AUGAACAU	10293
1864	GUCCUACU G UUCAAGCC	1632	GGCUUGAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGUAGGAC	10294
1881	UCCAAAGCU G UGCCUUGG	1633	CCAAGGCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGCUUGGA	10295
1939	GAGCUUCU G UGGAGUUA	1634	UAAUCUCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGAAGCUC	10296
2013	UCUGUCUC G UAUCGGGG	1635	CCCCGAUA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGAGCAGA	10297
2045	GGAACAU G UUCACCUC	1636	GAGGUGAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AAUGUUCU	10298
2082	GCUAUUCU G UGUUGGGG	1637	CCCCAACA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGAAUAGC	10299
2084	UAUUCUGU G UUGGGGUG	1638	CACCCCAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG ACAGAAUA	10300
2167	UCAGGUAU G UCAACGUU	1639	AACGUUGA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AUAGCUGA	10301
2205	CAACUAU G UGGUUUCA	1640	UGAAACCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AAUAGUUG	10302
2222	CAUUUCCU G UCUIUACU	1641	AAGUAAGA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGGAAAUG	10303
2245	GAGAAACU G UUCUUGAA	1642	UUCAAAGAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGUUUCUC	10304
2262	UAUUUGGU G UCUIUUGG	1643	CCAAAAGA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG ACCAAUAU	10305
2274	UUUGGAGU G UGGAUUGG	1644	CGAAUCCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG ACUCCAAA	10306
2344	AAACUACU G UUGUUAGA	1645	UCUAACAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGUAGUUU	10307
2347	CUACUGUU G UUAGAGGA	1646	UCGUCUAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AACAGUAG	10308
2450	AUCUCAU G UUAGUAUU	1647	AAUACUAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AUUGAGAU	10309
2573	AGGACAU G UUGAUAGA	1648	UCUAUCAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AAUGUCCU	10310
2583	UGAUAGAU G UAAGCAAU	1649	AUUGCUUA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AUCUAUCA	10311
2594	AGCAAUUU G UGGGGCCC	1650	GGGCCCCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AAUUGUCU	10312
2663	AUCCCAAU G UUAUAAAA	1651	UUUAGUAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AUUGGGAU	10313
2717	CAGAGUAU G UAGUUAAU	1652	AUUAACUA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AUACUCUG	10314
2901	AUCUUUCU G UCCCCAAU	1653	AUUGGGGA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGAAAGAU	10315
3071	GGGGGACU G UUGGGGUG	1654	CACCCCAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGUCCCCC	10316
3111	UCACAACU G UGCCAGCA	1655	UGCUGGCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG AGUUGUGA	10317
40	AUCCCAGA G UCAGGGCC	1656	GGCCCUGA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UCUGGGAU	10318
46	GAGUCAGG G CCCUGUAC	1657	GUACAGGG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CCUGACUC	10319
65	UCCUGCUG G UGGCUCCA	1658	UGGAGCCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CAGCAGGA	10320
68	UGCUGGUG G CUCCAGUU	1659	AACUGAG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CACCAGCA	10321
74	UGGCUCCA G UUCAGGAA	1660	UUCUUGAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UGGAGCCA	10322
85	CAGGAACA G UGAGCCCU	1661	AGGGCUCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UGUUCCUG	10323
89	AACAGUGA G CCCUGCUC	1662	GAGCAGGG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UCACUGUU	10324
120	GCCAUUUC G UCAAUCUU	1663	AAGAUUGA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GAUAUGGC	10325
196	CCCUGCUC G UGUUACAG	1664	CUGUAACA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GAGCAGGG	10326
205	UGUUACAG G CGGGGUTU	1665	AAACCCCG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CUGUAACA	10327

210	CAGGCGGG G UUUUUCUU	1666	AAGAAAA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CCCGCCUG	10328
248	ACCACAGA G UCUAGACU	1667	AGUCUAGA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UCUGUGGU	10329
258	CUAGACUC G UGGUGGAC	1668	GUCCACCA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG GAGUCUAG	10330
261	GACUCGUG G UGGACUUC	1669	GAAGUCCA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CACGAGUC	10331
295	GAACACCC G UGUGUCUU	1670	AAGACACA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG GGGUGUUC	10332
305	GUGUCUUG G CCAAAAUU	1671	AAUUUGG GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CAAGACAC	10333
318	AAUUGGCA G UCCCAAUU	1672	AUUUGGA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UCGAAUUU	10334
332	AAUCUCCA G UCACUCAC	1673	GUGAGUA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UGGAGAUU	10335
368	UUGUCCUG G UUAUCGCU	1674	AGCGAUA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CAGGACAA	10336
390	UGUCUGCG G CGUUUUUU	1675	AUAAACG GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CGCAGACA	10337
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461	CUAUAAG G UAUGUUGC	1678	GCAACUA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CUUGAUAG	10340
472	UGUUGCCC G UTUUGCCU	1679	AGGACAA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG GGGCAACA	10341
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625	CAUCUUGG G CUUUQCGA	1681	UGCAGAG GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CCAAGAUG	10343
648	CUAUGGGA G UGGGCCUC	1682	GAGGCCA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UCCCAUAG	10344
652	GGGAGUGG G CCUCAGUC	1683	GACUGAG GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CCACUCCC	10345
658	GGGCCUCA G UCCGUUUC	1684	GAACGGA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UGAGGCCC	10346
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672	UUCUCUUG G CUCAGUUU	1686	AAACUGAG GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CAAGAGAA	10348
677	UUGGCUCA G UUUACUAG	1687	CUAGUAA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UGAGCCAA	10349
685	GUUUACUA G UGCCAUUU	1688	AAUUGGA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UAGUAAAC	10350
699	UUUGUUCA G UGGUUCGU	1689	ACGAACA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UGAACAAA	10351
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711	UUCGUAGG G CUUUCCCC	1692	GGGAAAG GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CCUACGAA	10354
729	ACUGUCUG G CUUUCAGU	1693	ACUGAAG GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CAGACAGU	10355
736	GGCUUUCA G UUAUAUGG	1694	CCAUUAA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UGAAAGCC	10356
753	AUGAUGUG G UTUUGGGG	1695	CCCCAAA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CACAUCAU	10357
762	UUUUGGGG G CCAAGUCU	1696	AGACUUG GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CCCCAGAA	10358
767	GGGCCCAA G UCUGUACA	1697	UGUACAGA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UUGGCCCC	10359
785	CAUCUUGA G UCCCUUUA	1698	UAAAGGA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UCAAGAUG	10360
826	GUCUUUGG G UAUACAUI	1699	AAUGUA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CCAAAGAC	10361
898	AAUUGGGA G UUGGGGCA	1700	UGCCCCA GGAGAAACUCC CU UCAAGGACAUCGUCCGGG UCCCAAUU	10362
904	GAGUUGGG G CACAUUGC	1701	GCAUGUG GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CCCAACUC	10363
971	GUAAACAG G CCUAUUGA	1702	UCAUAGG GGAGAAACUCC CU UCAAGGACAUCGUCCGGG CUGUUUAC	10364

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1016	CUUUUGG G UUUGCGC	1705	GGGGCAA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CCCAAAAG	10367
1080	GCAUACAA G CAAAACAG	1706	CUGUUUG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG UUGUAUGC	10368
1089	CAAAACAG G CUUUUACU	1707	AGUAAAAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CUGUUUUG	10369
1116	CUUACAAG G CCUUUCUA	1708	UAGAAAGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CUUGUAAAG	10370
1126	CUUUCUAA G UAAACAGU	1709	ACUGUUUA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG UUAGAAAAG	10371
1133	AGUAAAAC G UAUGUGAA	1710	UUCACAU A GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG UGUUUACU	10372
1152	UUUACCCC G UUGCUCGG	1711	CCGAGCAA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GGGGUAAA	10373
1160	GUUGUCG G CAACGGCC	1712	GGCCGUUG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CGAGCAAC	10374
1166	CGGCAACG G CCUGGUCU	1713	AGACCAGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CGUUGCCG	10375
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1207	CCCCACUG G UUGGGGCU	1716	AGCCCCAA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CAGUGGGG	10378
1213	UGGUUGG G CUUGGCCA	1717	UGGCCAAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CCCAACCA	10379
1218	GGGGCUUG G CCAUAGGC	1718	GCCUAUGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CAAAGCCC	10380
1225	GGCCAUAG G CCAUCAGC	1719	GCUGAUGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CUAUGGCC	10381
1232	GGCCAUCA G CGCAUGCG	1720	CGCAUGCG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG UGAUGGCC	10382
1240	GGCAUGC G UGGAACCU	1721	AGGUUCCA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GCAUGCGC	10383
1287	AACUCCUA G CCGCUUGU	1722	ACAAGCGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG UAGGAGUU	10384
1306	UGCUCGCA G CAGGUCUG	1723	CAGACCTUG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG UGCAGAGCA	10385
1310	CGCAGCAG G UCUGGGGC	1724	GCCCCAGA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CUGCUGCG	10386
1317	GGUCUGGG G CAAAACUC	1725	GAGUUUUG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CCCAGACC	10387
1347	AUUCUGUC G UGCUCUCC	1726	GGAGAGCA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GACAGAAU	10388
1379	UUUCCAUG G CUGCUAAG	1727	CCUAGCAG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CAUGGAAA	10389
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1418	CGCGGGAC G UCCUUUGU	1729	ACAAAGGA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GUCCCGCG	10391
1431	UUGUUUAC G UCCCGUCG	1730	CGACGGGA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GUAAACAA	10392
1436	UACGUCCC G UCGGGGCU	1731	AGGCCGA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GGGACGUA	10393
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1471	CUCCGGGG G CCGCUUGG	1733	CCAAGCGG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CCCGGGAG	10395
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1517	UACCGACC G UCCACGGG	1735	CCCGUGGA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GGUCGGUA	10397
1526	UCCACGGG G CGCACUCU	1736	GAGGUGCG GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CCCGUGGA	10398
1553	GACUCCCC G UCUGUGCC	1737	GGCACAGA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GGGGAGUC	10399
1579	GCCGGACC G UGUGCACU	1738	AGUGCACA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GGUCCGGC	10400
1605	CUCUGCAC G UCGCAUGG	1739	CCAUGCGA GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GUGCAGAG	10401

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1679	GACUUUA G CAUUGUCA	1742	UGACAUUG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UGAAAAGUC	10404
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1732	UUUAUUA G UGGGAGGA	1744	UCCUCCCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UCAUUAUAA	10406
1741	UGGGAGGA G UUGGGGGA	1745	UCCCCCAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UCCUCCCA	10407
1754	GGGAGGAG G UUAGGUUA	1746	UAACCUAA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CUCCUCCC	10408
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1789	GGCUGUAG G CAUAAAUU	1750	AAUUUAUG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CUACAGCC	10412
1799	AUAAUUG G UGUGUUA	1751	UGAACACA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CAAUUUAU	10413
1811	GUUCACCA G CACCAUGC	1752	GCAUGGUG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UGGUGAAC	10414
1870	CUGUJCAA G CCUCCAAG	1753	CUUGGAGG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UUGAACAG	10415
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1890	UGCCUUGG G UGGCUUUG	1755	CAAGCCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CCAAGGCA	10417
1893	CUUGGGUG G CUUUGGGG	1756	CCCCAAG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CACCCAAG	10418
1901	GCUUUGGG G CAUGGACA	1757	UGUCCAUG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CCCAAAGC	10419
1917	AUGACCC G UAUAAGA	1758	UCUUUA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GGUCAAU	10420
1933	AUUUGGA G CUUCUGUG	1759	CACAGAAG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UCCAAAUU	10421
1944	UCUGUGGA G UUAUCUC	1760	GAGAUUA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UCCACAGA	10422
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2031	GCCUUAGA G UCUCGGA	1762	UCCGGAGA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UCUAAGGC	10424
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2070	GCACUCAG G CAAGCUAU	1764	AUAGCUUG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CUGAGUGC	10426
2074	UCAGGCAA G CUAUUCUG	1765	CAGAAUAG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UUGCCUGA	10427
2090	GUGUUGGG G UGAGUUGA	1766	UCAACUCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CCCAACAC	10428
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2107	UGAAUCUA G CCACCUUG	1768	CCAGGUGG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UAGAUIUA	10430
2116	CCACCUUG G UGGGAAGU	1769	ACUUCCCA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CCAGGUGG	10431
2123	GGUGGGAA G UAAUJUGG	1770	CCAAAUUA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UUCCCACC	10432
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2155	GGGAAUUA G UAGUCAGC	1772	GCUGACUA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UAAUCCCC	10434
2158	AUUUAGUA G UCAGCUAU	1773	AUAGCUGA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UACUAAUU	10435
2162	AGUAGUCA G CUAUGUCA	1774	UGACAUAG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG UGACUACU	10436
2173	AUGUCAAC G UUAUAUUG	1775	CAUAUUA GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG GUUGACAU	10437
2183	UAAUAUGG G CCUAAAAA	1776	UUUUUAGG GGAGGAAAACUCC CU UCAAGGACAUCGUCCGGG CCAUAUUA	10438

2208	CUAUUG G UUUCACAU	1777	AUGUGAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CACAAUAG	10439
2235	ACUUUGG G CGAGAAC	1778	GUUUCUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAAAAGU	10440
2260	AAUAUUG G UGUCUUUU	1779	AAAAGACA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAAAUUUU	10441
2272	CUUUUGA G UGUGGAU	1780	AAUCCACA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UCCAAAAG	10442
2360	ACGAAGAG G CAGGUCCC	1781	GGGACCUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUUUCUGU	10443
2364	AGAGGAG G UCCCUUAG	1782	CUAGGGGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUGCCUCU	10444
2403	AGACGAAG G UCUCAAUC	1783	GAUUGAGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUUCGUCU	10445
2417	AUCGCCG G UCGAGAA	1784	UUCUGCGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GCGGCGAU	10446
2454	CAAUUUA G UAUUCCUU	1785	AAGGAUUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UAACAUUG	10447
2474	CACAUAG G UGGGAAAC	1786	GUUUCCCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUUAUGUG	10448
2491	UUUACGG G CUUUAUUC	1787	GAUUAAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCGUAAAA	10449
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2530	CCUAAAUG G CAAACUCC	1789	GGAGUUUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAUUUAGG	10451
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2599	UUUGUGG G CCCUUUAC	1791	GUUAGGGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCCACAAA	10453
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2650	CCUGCUAG G UUUUAUCC	1793	GGUAUAAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUAGCAGG	10455
2701	AUCAAACC G UAUUAUCC	1794	GGUAUUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GGUUUGAU	10456
2713	UAUCCAGA G UAUUGAU	1795	ACUACUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UCUGGAUA	10457
2720	AGUAUGUA G UUAUCAU	1796	AUGAUUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UACAUACU	10458
2768	UUUGAAG G CGGGAUUC	1797	GAUCCCGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUUCCAAA	10459
2791	AAAAGAGA G UCCACACG	1798	CGUGUGGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UCUCUUUU	10460
2799	GUCCACAC G UAGCGCCU	1799	AGGCGCUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GUGUGGAC	10461
2802	CACACGUA G CGCCUCAU	1800	AUGAGGCG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UACGUGUG	10462
2818	UUUUGCGG G UCACCAUA	1801	UAUGGUGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCGCAAAA	10463
2848	GAUCUACA G CAUGGGAG	1802	CUCCCAUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGUAGAUC	10464
2857	CAUGGGAG G UUGGUUUU	1803	AAGACCAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUCCCAUG	10465
2861	GGAGGUUG G UCUUCCAA	1804	UUGGAAGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAACCUCC	10466
2881	UCGAAAAG G CAUGGGGA	1805	UCCCAUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUUUUCGA	10467
2936	GAUCAUA G UUGGACCC	1806	GGGUCCAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGAUGAUC	10468
2955	CAUUCAAA G CCAACUCA	1807	UGAUUUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UUUUGAUG	10469
2964	CCAACUCA G UAAAUCCA	1808	UGGAUUUA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGAGUUGG	10470
3005	GACAAACUG G CCGGACGC	1809	CGUCCGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAGUUGUC	10471
3021	CCAACAAG G UGGGAGUG	1810	CACUCCCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUUGUUGG	10472
3027	AGGUGGGA G UGGGAGCA	1811	UGCUCCCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UCCCACCU	10473
3033	GAGUGGGA G CAUUCGGG	1812	CCCGAUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UCCCACUC	10474
3041	GCAUUCGG G CCAGGGUU	1813	AACCCUGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCGAAUUC	10475

3047	GGCCAGG G UUCACCCC	1814	GGGUGAA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCUGGCCC	10476
3077	CUGUUGG G UGGAGCCC	1815	GGGCUCCA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCCAACAG	10477
3082	GGGUGGA G CCUCACG	1816	CGUGAGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UCCACCCC	10478
3097	CGUCAGG G CCUACUA	1817	UGAGUAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCUGAGCG	10479
3117	CUGUGCCA G CAGCUCCU	1818	AGGAGCUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGGCACAG	10480
3120	UGCCAGCA G CUCCUCCU	1819	AGGAGGAG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGCUGGCA	10481
3146	ACCAAUC G CAGUCAGG	1820	CCUGACUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CGAUUGGU	10482
3149	AAUCGGCA G UCAGGAAG	1821	CUUCCUGA GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGCCGAUU	10483
3158	UCAGGAAG G CAGCCUAC	1822	GUAGGCUG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUUCCUGA	10484
3161	GGAAGGCA G CCUACUCC	1823	GGAGUAGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGCCUUCC	10485
3204	AUCCUCAG G CCAUGCAG	1824	CUGCAUGG GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUGAGGAU	10486
31	CUCUCAA G AUCCGAGA	1999	UCUGGGAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UUGAAGAG	10487
38	AGAUCCCA G AGUCAGGG	2000	CCUGACU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGGGAUCU	10488
44	CAGAGUCA G GGCCCUGU	2001	ACAGGGCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGACUCUG	10489
45	AGAGUCAG G GCCCUGUA	2002	UACAGGGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUGACUCU	10490
64	UUCUUGCU G GUGGCUCC	2003	GGAGCCAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGCAGGAA	10491
67	CUGCUGGU G GCUCAGU	2004	ACUGGAGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACCAGCAG	10492
79	CCAGUUCA G GAACAGUG	2005	CACUGUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGAACUGG	10493
80	CAGUUCAG G AACAGUGA	2006	UCACUGUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUGAACUG	10494
99	CCUGCUCA G AAUACUGU	2007	ACAGUAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGAGCAGG	10495
135	UUAUCGAA G ACUGGGGA	2008	UCCCCAGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UUCGAUAA	10496
139	CGAAGACU G GGGACCCU	2009	AGGGUCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGUUCUUG	10497
140	GAAGACUG G GGACCCUG	2010	CAGGGUCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAGUCUUC	10498
141	AAGACUGG G GACCCUGU	2011	ACAGGGUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAGUCUU	10499
142	AGACUGGG G ACCCUGUA	2012	UACAGGGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCCAGUCU	10500
159	CCGAACAU G GAGAACAU	2013	AUGUUCUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUGUUCGG	10501
160	CGAACAU G AGAACAU	2014	GAUGUUCU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAUGUUCG	10502
162	AACAUGGA G AACAUCCG	2015	GCGAUGUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UCCAUGUU	10503
175	UCGCAUCA G GACUCCUA	2016	UAGGAGUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGAUGCGA	10504
176	CGCAUCAG G ACUCCUAG	2017	CUAGGAGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUGAUGCG	10505
184	GACUCCUA G GACCCUG	2018	CAGGGUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UAGGAGUC	10506
185	ACUCCUAG G ACCCUGC	2019	GCAGGGUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUAGGAGU	10507
204	GUGUUACA G GCGGGGUU	2020	AACCCCGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGUAAAC	10508
207	UACAGGC G GGGUUUUU	2021	AAAAACCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GCCUGUAA	10509
208	UACAGGC G GGUUUUUC	2022	GA AAAACC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CGCCUGUA	10510
209	ACAGGCG G GUUUUUUC	2023	AGAAAAAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCGCCUGU	10511
246	AUACCACA G AGUCUAGA	2024	UCUAGACU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGUGGUAU	10512

253	AGAGUCUA G ACUCGUGG	2025	CCACGAGU GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG UAGACUCU	10513
260	AGACUCGU G GUGGACUU	2026	AAGUCCAC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG ACGAGUCU	10514
263	CUCGUGGU G GACUUCUC	2027	GAGAAGUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG ACCACGAG	10515
264	UCGUGGUG G ACUUCUCU	2028	AGAGAAGU GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CACCACGA	10516
283	AUUUUCUA G GGGGAACA	2029	UGUUCGCC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG UAGAAAAU	10517
284	UUUUCUAG G GGAACACC	2030	GUGUUCGC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CUAGAAAA	10518
285	UUUCUAGG G GGAACACC	2031	GGUGUUCG GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CCUAGAAA	10519
286	UUCUAGGG G GAACACCC	2032	GGGUGUUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CCCUAGAA	10520
287	UCUAGGGG G AACACCCG	2033	CGGGUGUU GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CCCUAGA	10521
304	UGUGUCUU G GCCAAAAU	2034	AUUUUGGC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG AAGACACA	10522
367	UUUGUCCU G GUUAUCGC	2035	GCGAUAAC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG AGGACAAA	10523
377	UUAUGGCU G GAUGUGUC	2036	GACACAUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG AGCGAUAA	10524
378	UAUCGCUG G AUGUGUCU	2037	AGACACAU GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CAGCGAUA	10525
389	GUGUCUGC G GCGUUUUA	2038	UAAAACGC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG GCAGACAC	10526
441	UUCUUGUU G GUUCUUCU	2039	AGAAGAAC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG AACAGGAA	10527
450	GUUCUUCU G GACUAUCA	2040	UGAUAUUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG AGAAGAAC	10528
451	UUCUUCUG G ACUAUCA	2041	UUGAUAUG GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CAGAAGAA	10529
460	ACUAUCA G GUAUGUUG	2042	CAACAUAU GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG UUGAUAGU	10530
490	UAAUCCA G GAUCAUCA	2043	UGAUAUUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG UGGAUUUA	10531
491	AUUUCCAG G AUCAUCA	2044	UUGAUAUG GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CUGGAAUU	10532
511	CCAGCACC G GACCAUGC	2045	GCAUGGUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG GGUGCUGG	10533
512	CAGCACCG G ACCAUGCA	2046	UGCAUGGU GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CGGUGCUG	10534
544	CUGUCUAA G GAACCUCU	2047	AGAGGUUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG UUGAGCAG	10535
545	UGUCUAAG G AACUCUA	2048	UAGAGGUU GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CUUGAGCA	10536
585	AAACCUAC G GACGGAAA	2049	UUUCCGUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG GUAGGUUU	10537
586	AACCUACG G ACGGAAAC	2050	GUUUCCGU GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CGUAGGUU	10538
589	CUACGGAC G GAAACUGC	2051	GCAGUUUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG GUCCGUAG	10539
590	UACGGACG G AAACUGCA	2052	UGCAGUUU GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CGUCCGUA	10540
623	AUCAUCUU G GGCUUUCG	2053	CGAAAGCC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG AAGAUGAU	10541
624	UCAUCUUG G GCUUUCGC	2054	GCGAAAGC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CAAGAUGA	10542
644	AUACCUAU G GGAGUGGG	2055	CCCACUCC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG AUAGGUUU	10543
645	UACCUAUG G GAGUGGGC	2056	GCCCAUUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CAUAGGUA	10544
646	ACCUAUGG G AGUGGGCC	2057	GGCCCAUUC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CCAUAGGU	10545
650	AUGGGAGU G GGCCUCAG	2058	CUGAGGCC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG ACUCCCAU	10546
651	UGGGAGUG G GCCUCAGU	2059	ACUGAGGC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG CACUCCCA	10547
671	UUUCUCUU G GCUCAGUU	2060	AACUGAGC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG AAGAGAAA	10548
701	UGUUCAGU G GUUCGUAG	2061	CUACGAAC GGAGGAAAACUCC CU UCAAGGACAUUCGUCCGGG ACUGAACA	10549

709	GGUUCGUA G GGCUUUCC	2062	GGAAAGCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UACGAACC	10550
710	GUUCGUAG G GCUUCCCC	2063	GGGAAAGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUACGAAC	10551
728	CACUGUCU G GCUUUCAG	2064	CUGAAAGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGACAGUG	10552
743	AGUUAUUAU G GAUGAUGU	2065	ACAUAUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUUAUAACU	10553
744	GUUAUAUG G AUGAUGUG	2066	CACAUAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAUAUAAC	10554
752	GAUGAUGU G GUUUUGGG	2067	CCCAAAAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACAUCAUC	10555
758	GUGGUUUU G GGGGCCAA	2068	UUGCCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAAACCAC	10556
759	UGGUUUUG G GGGCCAAAG	2069	CUUGCCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAAAACCA	10557
760	GGUUUUUG G GGCCAAAGU	2070	ACUUGGCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAAAAACC	10558
761	GUUUUGGG G GCCAAGUC	2071	GACUUGGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAAAAAC	10559
824	UUGUCUUU G GGUUAACA	2072	UGUAUAAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAAGACAA	10560
825	UGUCUUUG G GUUAUACAU	2073	AUGUAUAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAAAGACA	10561
856	AACAAAAA G AUGGGGAU	2074	AUCCCCAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UUUUUGUU	10562
859	AAAAAGAU G GGAUAUU	2075	AAUAUCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUCUUUUU	10563
860	AAAAGAU G GGAUAUUC	2076	GAUAUCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAUCUUUU	10564
861	AAAGAUG G GAUAUUC	2077	GGAAUAUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAUCUUU	10565
862	AAGAUGG G AUAUUCCC	2078	GGGAUAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAUCUUU	10566
881	AACUUCAU G GGAUAUGU	2079	ACAUAUCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUGAAGUU	10567
882	ACUUCAG G GAUAUGUA	2080	UACAUAUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAUGAAGU	10568
883	CUUCAUGG G AUUGUA	2081	UUACAUAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAUGAAG	10569
894	AUGUAUUU G GGAGUUGG	2082	CCAACUCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAUUACA	10570
895	UGUAAUUG G GAGUUGGG	2083	CCCAACUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAAUUACA	10571
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902	GGGAGUUG G GGCACA	2086	AAUGUGCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAAUCUCC	10574
903	GGAGUUGG G GCACAUG	2087	CAAUGUGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAACUCC	10575
917	UUGCCACA G GAACAUAU	2088	AUAUGUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGUGGCAA	10576
918	UGCCACAG G AACAUUAU	2089	AAUAUGUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUGUGGCA	10577
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953	UGUUUUG G AAACUUC	2091	GGAGUUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUAAAAAC	10579
970	UGUAAACA G GCCUAUUG	2092	CAUAAGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGUUUACA	10580
982	UAUUGAUU G GAAAGUAU	2093	AUACUUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAUCAUA	10581
983	AUUGAUG G AAAGUAUG	2094	CAUACUUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAAUCAA	10582
1004	CGAAUUGU G GGUCUUUU	2095	AAAAGAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACAAUUCG	10583
1005	GAAUUGUG G GUCUUUUG	2096	CAAAAGAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CACAAUUC	10584
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1088	GCAAAACA G GCUUUUAC	2102	GUAAAAGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGUUUUGC	10590
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1210	CACUGGUU G GGGCUUGG	2108	CCAAGCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AACCAUG	10596
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1217	UGGGGCUU G GCCAUAGG	2111	CCUAUGGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAGCCCCA	10599
1224	UGGCCAUA G GCCAUCAG	2112	CUGAUGGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UAUUGGCA	10600
1242	GCAUGCGU G GAACCUUU	2113	AAAGGUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACGCAUGC	10601
1243	CAUGCGUG G AACCUUUG	2114	CAAGGUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CACGCAUG	10602
1277	CAUACCGC G GAACUCCU	2115	AGGAGUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GCGGUUUG	10603
1278	AUACCGCG G AACUCCUA	2116	UAGGAGUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CGCGGUUU	10604
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1314	GCAGGUCU G GGGCAAAA	2118	UUUUGCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGACCUGC	10606
1315	CAGGUCUG G GGCAAAAC	2119	GUUUUGCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAGACCUG	10607
1316	AGGUCUGG G GCAAAACU	2120	AGUUUUGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAGACCU	10608
1329	AACUCAUC G GGACUGAC	2121	GUCAGUCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GAUGAGUU	10609
1330	ACUCAUCG G GACUGACA	2122	UGUCAGUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CGAUGAGU	10610
1331	CUCAUCGG G ACUGACAA	2123	UUGUCAGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCGAUGAG	10611
1378	AUUUCCAU G GCUUCUAG	2124	CUAGCAGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUGGAAAU	10612
1386	GGCUGCUA G GCUUGUCU	2125	AGCAGAGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UAGCAGCC	10613
1402	UGCCAACU G GAUCCUAC	2126	GUAGGAUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGUUGGCA	10614
1403	GCAACUG G AUCCUACG	2127	CGUAGGAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAGUUGGC	10615
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1414	CCUACGCG G GACGUCCU	2129	AGGACGUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CGCGUAGG	10617
1415	CUACGGCG G ACGUCCUU	2130	AAGGACGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCGCGUAG	10618
1439	GUCCCGUC G GCGCUGAA	2131	UUCAGCGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GACGGGAC	10619
1454	AAUCCCCG G GACGACCC	2132	GGGUGGUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GCGGGAAU	10620
1455	AUCCCGCG G ACGACCCC	2133	GGGGUCGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CGCGGGAU	10621
1468	CCCCUCCC G GGGCCGCU	2134	AGCGCCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GGGAGGGG	10622
1469	CCUCCCG G GGC CGCUU	2135	AAGCGGCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CGGGAGGG	10623

1470	CCUCCGG G GCGCUUG	2136	CAAGCGC GGAGAAACUCC CU UCAAGGACAUCGUCCGG CCGGGAGG	10624
1478	GGCGGCU G GGGUCUA	2137	UAGAGCC GGAGAAACUCC CU UCAAGGACAUCGUCCGG AAGCGGCC	10625
1479	GCCGCUUG G GGCUCUAC	2138	GUAGAGC GGAGAAACUCC CU UCAAGGACAUCGUCCGG CAAGCGGC	10626
1480	CCGCUUG G GCUCUACC	2139	GGUAGAGC GGAGAAACUCC CU UCAAGGACAUCGUCCGG CCAAGCGG	10627
1523	CCGUCCAC G GGGCGCAC	2140	GUGCGCCC GGAGAAACUCC CU UCAAGGACAUCGUCCGG GUGGACGG	10628
1524	CGUCCACG G GCGGCACC	2141	GGUGCGC GGAGAAACUCC CU UCAAGGACAUCGUCCGG CGUGGACG	10629
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1545	UUUJACG G ACUCCCCG	2144	CGGGAGU GGAGAAACUCC CU UCAAGGACAUCGUCCGG CCGUAAAG	10632
1574	CAUCUGCC G GACCGUGU	2145	ACACGGU GGAGAAACUCC CU UCAAGGACAUCGUCCGG GGCAGAU	10633
1575	AUCUGCCG G ACCGUGUG	2146	CACACGU GGAGAAACUCC CU UCAAGGACAUCGUCCGG CGGCAGAU	10634
1612	CGUCGAU G GAGACCAC	2147	GUGGUCU GGAGAAACUCC CU UCAAGGACAUCGUCCGG AUGCGACG	10635
1613	GUCGAUG G AGACCACC	2148	GGUGGUC GGAGAAACUCC CU UCAAGGACAUCGUCCGG CAUGCAGC	10636
1615	CGCAUGGA G ACCACCGU	2149	ACGGUGU GGAGAAACUCC CU UCAAGGACAUCGUCCGG UCCAUGCG	10637
1635	CGCCACAC G GAACGUGC	2150	GCAGGUC GGAGAAACUCC CU UCAAGGACAUCGUCCGG UGUGGGCG	10638
1636	GCCACAG G AACGUGCC	2151	GGCAGGU GGAGAAACUCC CU UCAAGGACAUCGUCCGG CUGUGGGC	10639
1648	CUGCCAA G GUCUUGCA	2152	UGCAAGC GGAGAAACUCC CU UCAAGGACAUCGUCCGG UUGGGCAG	10640
1660	UUGCAUAA G AGGACUCU	2153	AGAGUCU GGAGAAACUCC CU UCAAGGACAUCGUCCGG UUAUGCAA	10641
1662	GCAUAGA G GACUCUUG	2154	CAAGAGU GGAGAAACUCC CU UCAAGGACAUCGUCCGG UCUUAUGC	10642
1663	CAUAAGAG G ACUCUUGG	2155	CCAAGAGU GGAGAAACUCC CU UCAAGGACAUCGUCCGG UCUUAUGC	10643
1670	GGACUCU G GACUUUCA	2156	UGAAAGU GGAGAAACUCC CU UCAAGGACAUCGUCCGG AAGAGUCC	10644
1671	GACUCUUG G ACUUUCAG	2157	CUGAAAGU GGAGAAACUCC CU UCAAGGACAUCGUCCGG CAAGAGUC	10645
1702	GACCUUGA G GCAUACUU	2158	AAGUAUGC GGAGAAACUCC CU UCAAGGACAUCGUCCGG UCAAGGUC	10646
1715	ACUUCAAA G ACUGUGUG	2159	CACACAGU GGAGAAACUCC CU UCAAGGACAUCGUCCGG UUUGAAGU	10647
1734	UAUAGAGU G GGAGGAGU	2160	ACUCCUC GGAGAAACUCC CU UCAAGGACAUCGUCCGG ACUCAUUA	10648
1735	AUUGAGUG G GAGGAGUU	2161	AACUCCU GGAGAAACUCC CU UCAAGGACAUCGUCCGG CACUCAUU	10649
1736	AUGAGUG G AGGAGUUG	2162	CAACUCCU GGAGAAACUCC CU UCAAGGACAUCGUCCGG CCACUCAU	10650
1738	GAGUGGGA G GAGUUGGG	2163	CCCAACU GGAGAAACUCC CU UCAAGGACAUCGUCCGG UCCACUC	10651
1739	AGUGGGAG G AGUUGGGG	2164	CCCCAACU GGAGAAACUCC CU UCAAGGACAUCGUCCGG CUCCACU	10652
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1751	UGGGGGAG G AGGUUAGG	2171	CUAACCU GGAGAAACUCC CU UCAAGGACAUCGUCCGG CUCCCCA	10659
1753	GGGAGGA G GUUAGGUU	2172	AACCUAAC GGAGAAACUCC CU UCAAGGACAUCGUCCGG UCCUCCCC	10660

1758	GGAGGUUA G GUUAAAGG	2173	CCUUUAAAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UAACCUCC	10661
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1778	UUGUACUA G GAGGCUGU	2175	ACAGCCUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UAGUACAA	10663
1779	UGUACUAG G AGGCUGUA	2176	UACAGCCU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUAGUACA	10664
1781	UACUAGGA G GCUGUAGG	2177	CCUACAGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UCCUAGUA	10665
1788	AGGCUGUA G GCAUAAAU	2178	AUUUAUGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UACAGCCU	10666
1798	CAUAAAUU G GUGUGUUC	2179	GAACACAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAUUUAUG	10667
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1889	GUGCCUUG G GUGGCUUU	2181	AAAGCCAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAAGGCAC	10669
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1898	GUGGCUUU G GGGCAUGG	2183	CCAUGCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAAGCCAC	10671
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1905	UGGGCAU G GACAUUGA	2186	UCAAUGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUGCCCCA	10674
1906	GGGCAUG G ACAUUGAC	2187	GUCAAUGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAUGCCCC	10675
1924	CGUUAUAA G AAUUUGGA	2188	UCCAAAUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UUUUAUACG	10676
1930	AAGAAUUU G GAGCUUCU	2189	AGAAGCUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AAUUCUU	10677
1931	AGAAUUUG G AGCUUCUG	2190	CAGAAACU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAAAUUCU	10678
1941	GCUUCUGU G GAGUUAU	2191	AGUAAACU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACAGAAGC	10679
1942	CUUCUGUG G AGUUAUC	2192	GAGUAAACU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CACAGAAG	10680
1987	CUAUUCGA G AUCUCCUC	2193	AGGCCCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GAUACAGA	10682
2018	UCUGUAUC G GGGGGCCU	2194	AAGGCCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CGAUACAG	10683
2019	CUGUAUCG G GGGGCCUU	2195	UAAGGCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCGAUACA	10684
2020	UGUAUCGG G GGGCCUUA	2196	CUAAGGCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCCGAUAC	10685
2021	GUUUCGGG G GGCCUUAG	2197	UCUAAGGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCCCGAUA	10686
2022	UAUCGGGG G GCCUUAGA	2198	CGGAGACU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UAAAGGCC	10687
2029	GGGCCUUA G AGUCUCCG	2199	CAAUGUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GGAGACUC	10688
2037	GAGUCUCC G GAACAUUG	2200	ACAAUGUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CGGAGACU	10689
2038	AGUCUCCG G AACAUUGU	2201	CUGAGUGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GUUUGGUG	10690
2061	CACCAUAC G GCACUCAG	2202	UAGCUUGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGAGUGCC	10691
2069	GGCACUCA G GCAAGCUA	2203	ACUCACCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AACACAGA	10692
2087	UCUGUGUU G GGGUGAGU	2204	AACUCACC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAACACAG	10693
2088	CUGUGUUG G GGUGAGUU	2205	CAACUCAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAACACA	10694
2089	UGUGUUGG G GUGAGUUG	2206	UUCCACCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AGGUGGCU	10695
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2115	GCCACCUG G GUGGGAAG	2208	UUACUCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACCCAGGU	10697
2118	ACCUUGGU G GGRAGUAA	2209		

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2120	CUGGGUG G AAGUAAU	2211	AAUUUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG CACCCAG	10699
2130	AGUAAUU G GAAGUCC	2212	GGAUUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGG AAUUUACU	10700
2131	GUAAUUU G AAGAUCA	2213	UGGAUUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG CAAAUUAC	10701
2134	AUUUGAA G AUCCAGCA	2214	UGCUGAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG UUCCAAU	10702
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2149	CAUCCAG G AAUUAGUA	2217	UACUAAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG CCUGGAUG	10705
2181	GUUAAU G GGCUAAA	2218	UUUAGGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGG AAUUAAC	10706
2182	UUAAUUG G GCUAAAA	2219	UUUAGGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGG CAUUAUAA	10707
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2234	UACUUUU G GCGAGAA	2223	UUUCUCG GGAGGAAACUCC CU UCAAGGACAUCGUCCGG CAAAAGUA	10711
2239	UUGGCGA G AAACUGUU	2224	AACAGUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG UGCCCCAA	10712
2259	GAUUAUU G GUGUCUUU	2225	AAAGAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGG AAUUAUUC	10713
2269	UGUCUUU G GAGUGUG	2226	CCACACU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG AAAAGACA	10714
2270	GUCUUUG G AGUGUGA	2227	UCCACACU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG CAAAAGAC	10715
2276	UGGAGUG G GAUUGCA	2228	UGCGAUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGG ACACUCCA	10716
2277	GGAGUG G AUUCGAC	2229	GUGCGAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG CACACUCC	10717
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2334	ACAUUCC G GAAACUAC	2231	GUAGUUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG GGAAGUGU	10719
2335	CACUCCG G AAACUACU	2232	AGUAGUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG CGGAAGUG	10720
2351	UGUUGUA G ACGAAGAG	2233	CUCUUGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG UAACAACA	10721
2357	UAGACGA G AGGAGGU	2234	ACCUGCU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG UUCGUUA	10722
2359	GACGAAG G GCAGGUCC	2235	GGACUCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGG UCUUCGUC	10723
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2372	GUCCCUA G AAGAAGAA	2237	UUCUUAU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG UAGGGAC	10725
2375	CCUAGAA G AAGAACUC	2238	GAGUUUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG UUCUAGG	10726
2378	UAGAAGAA G AACUCCU	2239	AGGAGUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGG UUCUUAU	10727
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2438	UCAUUC G GGAUUCU	2244	GAGAUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGG GAGAUUGA	10732
2439	CAUUCG G GAUUCUA	2245	UGAGUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGG CGAGUUG	10733
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2623	GAAACAG G AGACUUA	2267	UUAGUCC GGAGGAAACUCC CU UCAAGGACAUUGUCCGGG CUGUUUUC	10755
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2817	AUUUUGCG G GUCACCAU	2286	AUGGUGAC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CGCAAAAU	10774
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2833	UAUUCUUG G GAACAAGA	2288	UCUUGUUC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CAAGAAUA	10776
2834	AUUCUUGG G AACAGAU	2289	AUCUUGUU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CCAAGAAU	10777
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2915	AUUCUUUU G GGAUUCUU	2301	AAGAAUCC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGGGGAUU	10789
2916	AUCCCCUG G GAUUCUUC	2302	GAAGAAUC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CAGGGGAU	10790
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2940	AUCAGUUG G ACCUGCA	2305	UGCAGGUU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CAACUGAU	10793
2973	UAAAUCCA G AUUGGGAC	2306	GUCCCAAU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG UGGAUUUA	10794
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2996	CCGCACAA G GACAACUG	2310	CAGUUGUC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG UUGUGCGG	10798
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3004	GGACAACU G GCCGGACG	2312	CGUCCGGC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG AGUUGUCC	10800
3008	AACUGGCC G GACGCCAA	2313	UUGGGGUC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG GGCCAGUU	10801
3009	ACUGGCCG G ACGCCAAC	2314	GUUGGGU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CGGCCAGU	10802
3020	GCCAACAA G GUGGGAGU	2315	ACUCCAC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG UUGUUGGC	10803
3023	AACAAGGU G GGAGUGGG	2316	CCCACUCC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG ACCUUGUU	10804
3024	ACNAGGUG G GAGUGGGA	2317	UCCACUC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CACCUIUG	10805
3025	CAAGGUGG G AGUGGGAG	2318	CUCCACU GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CCACCUUG	10806
3029	GUGGGAGU G GGAGCAUU	2319	AUUGCUCC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG ACUCCAC	10807
3030	UGGAGUG G GAGCAUUC	2320	GAUUCUC GGAGGAAAACUCC CU UCAAGGACAUUGUCCGGG CACUCCCA	10808

3031	GGGAGUGG G AGCAUUG	2321	CGAAUGCU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCACUCC	10809
3039	GAGCAUUC G GGCCAGGG	2322	CCCUGGCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GAAUGCUC	10810
3040	AGCAUUG G GCCAGGGU	2323	ACCCUGGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CGAAUGCU	10811
3045	UCGGGCCA G GGUUCACC	2324	GGUGAAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGGCCCCG	10812
3046	CGGGCCAG G GUUCACCC	2325	GGUGAAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUGGCCCG	10813
3063	CUCCCAU G GGGGACUG	2326	CAGUCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AUGGGGAG	10814
3064	UCCCAUG G GGGACUGU	2327	ACAGUCCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAUGGGGA	10815
3065	CCCACUG G GGACUGUU	2328	AACAGUCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAUGGGG	10816
3066	CCCAUGG G GACUGUUG	2329	CAACAGUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAUGGG	10817
3067	CCAUGGG G ACUGUUGG	2330	CCAACAGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCCC AUGG	10818
3074	GGACUGUU G GGGUGGAG	2331	CUCCACCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG AACAGUCC	10819
3075	GACUGUUG G GGUGAGC	2332	GUCCACCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CAACAGUC	10820
3076	ACUGUUG G GUGAGCC	2333	GGCUCAC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCAACAGU	10821
3079	GUUGGGU G GAGCCUC	2334	GAGGGCUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG ACCCCAA	10822
3080	UUGGGUG G AGCCUCA	2335	UGAGGGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CACCCAA	10823
3095	CACGCUCA G GGCUACU	2336	AGUAGGCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGAGCGUG	10824
3096	ACGCUCAG G GCCUACUC	2337	GAGUAGGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUGAGCGU	10825
3145	CACCAAUC G GCAGUCAG	2338	CUGACUGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG GAUUGGUG	10826
3153	GGCAGUCA G GAAGGCAG	2339	CUGCCUUC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGACUGCC	10827
3154	GCAGUCAG G AAGGCAGC	2340	GCUGCCUU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUGACUGC	10828
3157	GUCAGGAA G GCAGCCUA	2341	UAGGCUGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UUCUUGAC	10829
3187	ACCUCUAA G GGACACUC	2342	GAGUUGCC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UUAGAGGU	10830
3188	CCUCUAG G GACACUCA	2343	UGAGUUGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CUUAGAGG	10831
3189	CUUAAGG G ACACUCAU	2344	AUGAGUGU GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG CCUUAAGG	10832
3203	CAUCCUCA G GCCAUGCA	2345	UGAUGGC GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG UGAGGAUG	10833

Input Sequence = AF100308. Cut Site = YG/M or UG/U.

Stem Length = 8. Core Sequence = GGAGGAAACUCC CU UCAAGGACAUCGUCCGGG

AF100308 (Hepatitis B virus strain 2-18, 3215 bp)

Table XI: Human HBV Enzymatic Nucleic Acid and Target Sequence

Pos	SUBSTRATE	Seq ID	RPI#	Ribozyme Alias	ENZYMATIC NUCLEIC ACID	Seq ID
313	CCAAAU U CGCAGUC	2346	18157	HBV-313 Rz-7 RNA	GACUGCG CUGAUGAGGCCGUUAGGCCGAA AUUUUGG B	10834
327	CCAAAU C UCCAGUC	2347	18158	HBV-327 Rz-7 RNA	GACUGGA CUGAUGAGGCCGUUAGGCCGAA AUUUUGG B	10835
334	CUCAGU C ACUCACC	2348	18159	HBV-334 Rz-7 RNA	GGUGAGU CUGAUGAGGCCGUUAGGCCGAA ACUGGAG B	10836
408	UCUUCU C UGCAUCC	2349	18160	HBV-408 Rz-7 RNA	GGAUGCA CUGAUGAGGCCGUUAGGCCGAA AGGAAGA B	10837
557	UCUAUGU U UCCCUCA	2350	18161	HBV-557 Rz-7 RNA	UGAGGGA CUGAUGAGGCCGUUAGGCCGAA ACAUAGA B	10838
1255	UUUGUGU C UCCUCUG	2351	18162	HBV-1255 Rz-7 RNA	CAGAGGA CUGAUGAGGCCGUUAGGCCGAA ACACAAA B	10839
1538	CCUCUCU U UACGCGG	2352	18163	HBV-1538 Rz-7 RNA	CCGCGUA CUGAUGAGGCCGUUAGGCCGAA AGAGAGG B	10840
1756	AGGAGGU U AGGUUAA	2353	18164	HBV-1756 Rz-7 RNA	UUAACCU CUGAUGAGGCCGUUAGGCCGAA ACCUCCU B	10841
1861	AUGUCU A CUGUUCA	2354	18165	HBV-1861 Rz-7 RNA	UGAACAG CUGAUGAGGCCGUUAGGCCGAA AGGACAU B	10842
2504	UUCUUCU A CGGUACC	2355	18166	HBV-2504 Rz-7 RNA	GGUACCG CUGAUGAGGCCGUUAGGCCGAA AGAAGAA B	10843
10	CUCACCC A CUUUGCA	2356	18197	HBV-10 CHZ-7 RNA	UGGAAAG CUGAUGAGGCCGUUAGGCCGAA GGUGGAG B	10844
335	UCCAGUC A CUCACCA	2357	18198	HBV-335 CHZ-7 RNA	UGGUGAG CUGAUGAGGCCGUUAGGCCGAA GACUGGA B	10845
1258	GUGUCUC C UCUGCGG	2358	18199	HBV-1258 CHZ-7 RNA	CGGCAGA CUGAUGAGGCCGUUAGGCCGAA GAGACAC B	10846
2307	GACCACC A AAUGGCC	2359	18200	HBV-2307 CHZ-7 RNA	GGGCAUU CUGAUGAGGCCGUUAGGCCGAA GGUGGUC B	10847
347	UCACCAACCU G UUGUC	2360	18216	HBV-347 GC1.Rz-5/10 RNA	GACAA UGAUGGCAUGCACUAUGCGCG AGGUUGGUA B	10848
350	CAAACCUU G UCCUC	2361	18217	HBV-350 GC1.Rz-5/10 RNA	GAGGA UGAUGGCAUGCACUAUGCGCG AACAGGUUG B	10849
1508	UCCGCCUAU G UACCG	2362	18218	HBV-1508 GC1.Rz-5/10 RNA	CGGUA UGAUGGCAUGCACUAUGCGCG AAUAGGCCGA B	10850
234	AAUCCU C ACAUA	2363	18334	HBV-234 Rz-6 allyl stabl	u ₅ a ₅ u ₅ gu cUGAUGagccguuagggccGaa Aggaau B	10851
252	GAGUCU A GACUUG	2364	18335	HBV-252 Rz-6 allyl stabl	c ₅ g ₅ a ₅ g ₅ uc cUGAUGagccguuagggccGaa Agacuc B	10852
268	UGGACU U CUCUCA	2365	18337	HBV-268 Rz-6 allyl stabl	u ₅ g ₅ a ₅ g ₅ ag cUGAUGagccguuagggccGaa Agucca B	10853
280	AAUUU C UAGGGG	2366	18345	HBV-280 Rz-6 allyl stabl	c ₅ c ₅ c ₅ ua cUGAUGagccguuagggccGaa Aaaaau B	10854
313	CAAAU U CGCAGU	2367	18346	HBV-313 Rz-6 allyl stabl	a ₅ c ₅ u ₅ g ₅ cg cUGAUGagccguuagggccGaa Anuuug B	10855
395	GGGUU U UAUCAU	2368	18350	HBV-395 Rz-6 allyl stabl	a ₅ u ₅ g ₅ a ₅ ua cUGAUGagccguuagggccGaa Aacgcc B	10856
402	UAUCAU C UUCUUC	2369	18351	HBV-402 Rz-6 allyl stabl	g ₅ a ₅ g ₅ g ₅ aa cUGAUGagccguuagggccGaa Augaua B	10857
607	UGUAU C CCAUCC	2370	18355	HBV-607 Rz-6 allyl stabl	g ₅ g ₅ a ₅ u ₅ g ₅ g cUGAUGagccguuagggccGaa Auauca B	10858
697	UUUGU C AGUGGU	2371	18362	HBV-697 Rz-6 allyl stabl	a ₅ c ₅ a ₅ u ₅ cu cUGAUGagccguuagggccGaa Aacaaa B	10859
1539	UCUCU U ACGCGG	2372	18366	HBV-1539 Rz-6 allyl stabl	c ₅ c ₅ g ₅ c ₅ gu cUGAUGagccguuagggccGaa Aagaga B	10860
1599	UCACCU C UGCACG	2373	18367	HBV-1599 Rz-6 allyl stabl	c ₅ g ₅ u ₅ g ₅ ca cUGAUGagccguuagggccGaa Agguga B	10861
1607	GCACGU C GCAUGG	2374	18368	HBV-1607 Rz-6 allyl stabl	c ₅ c ₅ a ₅ u ₅ g ₅ c cUGAUGagccguuagggccGaa Acgugc B	10862
1833	UCACCU C UGCCUA	2375	18371	HBV-1833 Rz-6 allyl stabl	u ₅ a ₅ g ₅ g ₅ ca cUGAUGagccguuagggccGaa Agguga B	10863

2383	AGAACU C CCUCGC	2376	18374	HBV-2383 Rz-6 allyl1 stabl	g ₅ c ₅ g ₅ a ₅ gg	cUGAuGagccgcuuagggccGaa	Aguucu B	10864
2429	GAAGAU C UCAAUC	2377	18376	HBV-2429 Rz-6 allyl1 stabl	g ₅ a ₅ u ₅ u ₅ ga	cUGAuGagccgcuuagggccGaa	Aucuuc B	10865
2831	UAUUCU U GGAAC	2378	18379	HBV-2831 Rz-6 allyl1 stabl	g ₅ u ₅ u ₅ c ₅ c ₅ cc	cUGAuGagccgcuuagggccGaa	Agauua B	10866
430	UGCCUC A UCUUCU	2379	18391	HBV-430 CHz-6 allyl1 stabl	a ₅ g ₅ a ₅ a ₅ ga	cUGAuGagccgcuuagggccGaa	Iaggca B	10867
676	UGGUCU A GUUUA	2380	18396	HBV-676 CHz-6 allyl1 stabl	g ₅ u ₅ a ₅ a ₅ ac	cUGAuGagccgcuuagggccGaa	Iagcca B	10868
683	GUUUAU U AGUGCC	2381	18397	HBV-683 CHz-6 allyl1 stabl	g ₅ g ₅ c ₅ a ₅ c ₅ cu	cUGAuGagccgcuuagggccGaa	Iuaaac B	10869
1150	UUUAAC C CGUUGC	2382	18402	HBV-1150 CHz-6 allyl1 stabl	g ₅ c ₅ a ₅ a ₅ c ₅ g	cUGAuGagccgcuuagggccGaa	Iguaaa B	10870
1200	GCAACC C CCACUG	2383	18403	HBV-1200 CHz-6 allyl1 stabl	c ₅ a ₅ g ₅ u ₅ g ₅ g	cUGAuGagccgcuuagggccGaa	Iguugc B	10871
1201	CAACCC C CACUGG	2384	18404	HBV-1201 CHz-6 allyl1 stabl	c ₅ c ₅ a ₅ g ₅ u ₅ g	cUGAuGagccgcuuagggccGaa	Igguug B	10872
1444	CGGCGC U GAAUCC	2385	18405	HBV-1444 CHz-6 allyl1 stabl	g ₅ g ₅ a ₅ u ₅ uc	cUGAuGagccgcuuagggccGaa	Icgccg B	10873
1451	GAAUCC C GCGGAC	2386	18406	HBV-1451 CHz-6 allyl1 stabl	g ₅ u ₅ c ₅ c ₅ g ₅ c	cUGAuGagccgcuuagggccGaa	Igaauu B	10874
1533	CGCACC U CUCUUU	2387	18407	HBV-1533 CHz-6 allyl1 stabl	a ₅ a ₅ a ₅ g ₅ ag	cUGAuGagccgcuuagggccGaa	Iguugc B	10875
1600	CACCUC U GCACGU	2388	18410	HBV-1600 CHz-6 allyl1 stabl	a ₅ c ₅ g ₅ u ₅ g ₅ c	cUGAuGagccgcuuagggccGaa	Iaggug B	10876
1698	CCGACC U UGAGGC	2389	18411	HBV-1698 CHz-6 allyl1 stabl	g ₅ c ₅ c ₅ u ₅ ca	cUGAuGagccgcuuagggccGaa	Igucgg B	10877
1784	GGAGGC U GUAGGC	2390	18412	HBV-1784 CHz-6 allyl1 stabl	g ₅ c ₅ c ₅ u ₅ ac	cUGAuGagccgcuuagggccGaa	Iccucc B	10878
1829	UUUUUC A CCUCUG	2391	18414	HBV-1829 CHz-6 allyl1 stabl	c ₅ a ₅ g ₅ a ₅ g ₅ g	cUGAuGagccgcuuagggccGaa	Iaaaaa B	10879
1876	GCCUCC A AGCUGU	2392	18420	HBV-1876 CHz-6 allyl1 stabl	a ₅ c ₅ a ₅ g ₅ cu	cUGAuGagccgcuuagggccGaa	Igaggc B	10880
1880	CCAAGC U GUGCCU	2393	18422	HBV-1880 CHz-6 allyl1 stabl	a ₅ g ₅ g ₅ c ₅ ac	cUGAuGagccgcuuagggccGaa	Icuugg B	10881
218	UUUUUCU U GUUGACA	2394	18333	HBV-218 Rz-7 allyl1 stabl	u ₅ g ₅ u ₅ c ₅ aac	cUGAuGagccgcuuagggccGaa	Agaaaaa B	10882
257	CUAGACU C GUGGUGG	2395	18336	HBV-257 Rz-7 allyl1 stabl	c ₅ c ₅ a ₅ c ₅ cac	cUGAuGagccgcuuagggccGaa	Agucuag B	10883
268	GUGGACU U CUCUCAA	2396	18338	HBV-268 Rz-7 allyl1 stabl	u ₅ u ₅ g ₅ a ₅ gag	cUGAuGagccgcuuagggccGaa	Aguccac B	10884
269	UGGACUU C UCUCAAU	2397	18339	HBV-269 Rz-7 allyl1 stabl	a ₅ u ₅ u ₅ g ₅ a ₅ ga	cUGAuGagccgcuuagggccGaa	Agucca B	10885
271	GACUUCU C UCAAUUU	2398	18340	HBV-271 Rz-7 allyl1 stabl	a ₅ a ₅ a ₅ u ₅ uga	cUGAuGagccgcuuagggccGaa	Agaaugc B	10886
273	CUUCUCU C AAUUUUC	2399	18341	HBV-273 Rz-7 allyl1 stabl	g ₅ a ₅ a ₅ a ₅ auu	cUGAuGagccgcuuagggccGaa	Agagaag B	10887
277	UCUCAAU U UUCUAGG	2400	18342	HBV-277 Rz-7 allyl1 stabl	c ₅ c ₅ u ₅ a ₅ gaa	cUGAuGagccgcuuagggccGaa	Auugaga B	10888
278	CUCAAUU U UCUAGGG	2401	18343	HBV-278 Rz-7 allyl1 stabl	c ₅ c ₅ c ₅ u ₅ a ₅ ga	cUGAuGagccgcuuagggccGaa	Aauugag B	10889
279	UCAAAUU U CUAGGGG	2402	18344	HBV-279 Rz-7 allyl1 stabl	c ₅ c ₅ c ₅ c ₅ uag	cUGAuGagccgcuuagggccGaa	Aaauga B	10890
314	CAAAAUU C GCAGUCC	2403	18347	HBV-314 Rz-7 allyl1 stabl	g ₅ g ₅ a ₅ c ₅ ugc	cUGAuGagccgcuuagggccGaa	Aauuuug B	10891
385	GAUGUGU C UGCGGGG	2404	18348	HBV-385 Rz-7 allyl1 stabl	c ₅ g ₅ c ₅ c ₅ gca	cUGAuGagccgcuuagggccGaa	Acacauc B	10892
394	GCGGCGU U UUAUCAU	2405	18349	HBV-394 Rz-7 allyl1 stabl	a ₅ u ₅ g ₅ a ₅ uaa	cUGAuGagccgcuuagggccGaa	Acgccgc B	10893
402	UUUAUCAU C UUCCUCU	2406	18352	HBV-402 Rz-7 allyl1 stabl	a ₅ g ₅ a ₅ g ₅ gaa	cUGAuGagccgcuuagggccGaa	Augauaa B	10894
423	UGUGUCU A UGCCUCA	2407	18353	HBV-423 Rz-7 allyl1 stabl	u ₅ g ₅ a ₅ g ₅ gca	cUGAuGagccgcuuagggccGaa	Agcagca B	10895
429	UAUGCCU C AUCUUUC	2408	18354	HBV-429 Rz-7 allyl1 stabl	a ₅ g ₅ a ₅ a ₅ gau	cUGAuGagccgcuuagggccGaa	Aggcaua B	10896
679	GCUCAGU U UACUAGU	2409	18356	HBV-679 Rz-7 allyl1 stabl	a ₅ c ₅ u ₅ a ₅ g ₅ ua	cUGAuGagccgcuuagggccGaa	Acugagc B	10897

680	CUCAGUU U ACUAGUG	2410	18357	HBV-680 Rz-7 allyl stabl	C ₈ a ₈ C ₈ u ₈ agu	cUGAuGagccgguuaggccGaa	Aacugag B	10898
681	UCAGUUU A CUAGUGC	2411	18358	HBV-681 Rz-7 allyl stabl	G ₈ C ₈ a ₈ C ₈ uag	cUGAuGagccgguuaggccGaa	Aaacuga B	10899
684	GUUUACU A GUGCCAU	2412	18359	HBV-684 Rz-7 allyl stabl	a ₈ u ₈ g ₈ a ₈ g ₈ cac	cUGAuGagccgguuaggccGaa	Aguaaac B	10900
692	GUGCCAU U UGUUCAG	2413	18360	HBV-692 Rz-7 allyl stabl	C ₈ u ₈ g ₈ a ₈ aca	cUGAuGagccgguuaggccGaa	Auggcac B	10901
693	UGCCAUU U GUUCAGU	2414	18361	HBV-693 Rz-7 allyl stabl	a ₈ C ₈ u ₈ g ₈ aac	cUGAuGagccgguuaggccGaa	Aauggca B	10902
1534	CGCACCU C UCUUAC	2415	18363	HBV-1534 Rz-7 allyl stabl	G ₈ u ₈ a ₈ a ₈ saga	cUGAuGagccgguuaggccGaa	Aggugcg B	10903
1536	CACUCUC C UUUACGC	2416	18364	HBV-1536 Rz-7 allyl stabl	G ₈ C ₈ g ₈ u ₈ aaa	cUGAuGagccgguuaggccGaa	Agaggug B	10904
1538	CCUCUCU U UACGGCG	2352	18365	HBV-1538 Rz-7 allyl stabl	C ₈ C ₈ g ₈ C ₈ gua	cUGAuGagccgguuaggccGaa	Agagagg B	10905
1787	AGGCUGU A GGCAUAA	2417	18369	HBV-1787 Rz-7 allyl stabl	u ₈ u ₈ a ₈ u ₈ gcc	cUGAuGagccgguuaggccGaa	Acagccu B	10906
1793	UAGGCAU A AAUUGGU	2418	18370	HBV-1793 Rz-7 allyl stabl	a ₈ C ₈ S ₈ a ₈ suu	cUGAuGagccgguuaggccGaa	Augccua B	10907
1874	CAAGCCU C CAAGCUG	2419	18372	HBV-1874 Rz-7 allyl stabl	C ₈ a ₈ g ₈ C ₈ suu	cUGAuGagccgguuaggccGaa	Aggcuug B	10908
1887	UGUGCCU U GGGUGGC	2420	18373	HBV-1887 Rz-7 allyl stabl	G ₈ C ₈ C ₈ a ₈ ccc	cUGAuGagccgguuaggccGaa	Aggcaca B	10909
2383	AAGRAU C CCUCGCC	2421	18375	HBV-2383 Rz-7 allyl stabl	G ₈ g ₈ C ₈ a ₈ g ₈ agg	cUGAuGagccgguuaggccGaa	Aguucuu B	10910
2828	ACCAUUA U CUUGGGA	2422	18377	HBV-2828 Rz-7 allyl stabl	u ₈ C ₈ S ₈ C ₈ aag	cUGAuGagccgguuaggccGaa	Auauggu B	10911
2829	CCAUAU C UUGGGAA	2423	18378	HBV-2829 Rz-7 allyl stabl	u ₈ u ₈ C ₈ C ₈ caa	cUGAuGagccgguuaggccGaa	Auaugg B	10912
2831	AUAUUU C GGGAACA	2424	18380	HBV-2831 Rz-7 allyl stabl	u ₈ g ₈ u ₈ u ₈ ccc	cUGAuGagccgguuaggccGaa	Agaauu B	10913
256	UCUAGAC U CGUGGUG	2425	18381	HBV-256 CHz-7 allyl stabl	C ₈ a ₈ C ₈ C ₈ acg	cUGAuGagccgguuaggccGaa	Iucuaga B	10914
267	GGUGGAC U UCUCUCA	2426	18382	HBV-267 CHz-7 allyl stabl	u ₈ g ₈ g ₈ g ₈ saga	cUGAuGagccgguuaggccGaa	Iuccacc B	10915
270	GGACUUC U CUCAUUU	2427	18383	HBV-270 CHz-7 allyl stabl	a ₈ a ₈ u ₈ u ₈ gag	cUGAuGagccgguuaggccGaa	Iaagucc B	10916
272	ACUUCUC U CAAUUUU	2428	18384	HBV-272 CHz-7 allyl stabl	a ₈ a ₈ a ₈ a ₈ suu	cUGAuGagccgguuaggccGaa	Iagaagu B	10917
274	UUCUCUC A AUUUUCU	2429	18385	HBV-274 CHz-7 allyl stabl	a ₈ g ₈ a ₈ a ₈ suu	cUGAuGagccgguuaggccGaa	Iagagaa B	10918
386	AUGUGUC U GCGGCGU	2430	18386	HBV-386 CHz-7 allyl stabl	a ₈ C ₈ g ₈ C ₈ cgc	cUGAuGagccgguuaggccGaa	Iacacau B	10919
419	AUCCUGC U GCUAUGC	2431	18387	HBV-419 CHz-7 allyl stabl	G ₈ C ₈ a ₈ u ₈ agc	cUGAuGagccgguuaggccGaa	ICaggau B	10920
422	CUGCUGC U AUGCCUC	2432	18388	HBV-422 CHz-7 allyl stabl	G ₈ a ₈ g ₈ g ₈ scau	cUGAuGagccgguuaggccGaa	ICagcag B	10921
427	GCUAUGC C UCAUCUU	2433	18389	HBV-427 CHz-7 allyl stabl	a ₈ a ₈ g ₈ a ₈ uga	cUGAuGagccgguuaggccGaa	Icauagc B	10922
428	CUAUGCC U CAUCUUC	2434	18390	HBV-428 CHz-7 allyl stabl	G ₈ a ₈ a ₈ g ₈ aug	cUGAuGagccgguuaggccGaa	Igcauag B	10923
430	AUGCCUC A UCUUCUU	2435	18392	HBV-430 CHz-7 allyl stabl	a ₈ a ₈ g ₈ a ₈ saga	cUGAuGagccgguuaggccGaa	Iaggcau B	10924
608	UGUAUUC C CAUCCCA	2436	18393	HBV-608 CHz-7 allyl stabl	u ₈ g ₈ g ₈ g ₈ aug	cUGAuGagccgguuaggccGaa	Iaaauca B	10925
609	GUUAUCC C AUCCCAU	2437	18394	HBV-609 CHz-7 allyl stabl	a ₈ u ₈ g ₈ g ₈ gau	cUGAuGagccgguuaggccGaa	Igaauac B	10926
669	GUUUCUC U UGGCUCU	2438	18395	HBV-669 CHz-7 allyl stabl	u ₈ g ₈ a ₈ g ₈ cca	cUGAuGagccgguuaggccGaa	Iagaaac B	10927
689	CUAGUGC C AUUUGUU	2439	18398	HBV-689 CHz-7 allyl stabl	a ₈ a ₈ C ₈ a ₈ suu	cUGAuGagccgguuaggccGaa	Icacuag B	10928
690	UAGUGCC A UUUGUUC	2440	18399	HBV-690 CHz-7 allyl stabl	G ₈ s ₈ a ₈ g ₈ C ₈ aaa	cUGAuGagccgguuaggccGaa	Igcacua B	10929
718	GUUUUCC C CCACUGU	2441	18400	HBV-718 CHz-7 allyl stabl	a ₈ C ₈ a ₈ g ₈ ugg	cUGAuGagccgguuaggccGaa	Igaaagc B	10930
1149	CCUUUAC C CCGUUGC	2442	18401	HBV-1149 CHz-7 allyl stabl	G ₈ C ₈ a ₈ a ₈ C ₈ cg	cUGAuGagccgguuaggccGaa	Iuaaagg B	10931

1535	GCACCUC U CUUUACG	2443	18408	HBV-1535	CHz-7 allyl stabl	c ₉ s ₉ u ₉ a ₉ aag	cUGAUgagggccguuaggccGaa	Iagguc B	10932
1537	ACCUCUC U UUAACGG	2444	18409	HBV-1537	CHz-7 allyl stabl	c ₉ s ₉ c ₉ s ₉ uaa	cUGAUgagggccguuaggccGaa	Iagaggu B	10933
1791	UGUAGGC A UAAAUUG	2445	18413	HBV-1791	CHz-7 allyl stabl	c ₉ a ₉ a ₉ u ₉ uaa	cUGAUgagggccguuaggccGaa	Iccuaca B	10934
1831	UUUUCAC C UCUGCCU	2446	18415	HBV-1831	CHz-7 allyl stabl	a ₉ s ₉ g ₉ c ₉ s ₉ aga	cUGAUgagggccguuaggccGaa	Iugaaaa B	10935
1832	UUUCACC U CUGCCUA	2447	18416	HBV-1832	CHz-7 allyl stabl	u ₉ a ₉ g ₉ s ₉ cag	cUGAUgagggccguuaggccGaa	Igugaaa B	10936
1872	UUCAAAGC C UCCAAGC	2448	18417	HBV-1872	CHz-7 allyl stabl	g ₉ c ₉ s ₉ u ₉ gga	cUGAUgagggccguuaggccGaa	Icuugaa B	10937
1873	UCAAGCC U CCAAGCU	2449	18418	HBV-1873	CHz-7 allyl stabl	a ₉ s ₉ c ₉ s ₉ u ₉ gg	cUGAUgagggccguuaggccGaa	Igcuuga B	10938
1875	AAGCCUC C AAGCUGU	2450	18419	HBV-1875	CHz-7 allyl stabl	a ₉ c ₉ a ₉ s ₉ cuu	cUGAUgagggccguuaggccGaa	Iaggcuu B	10939
1876	AGCCUCC A AGCUGUG	2451	18421	HBV-1876	CHz-7 allyl stabl	c ₉ a ₉ c ₉ s ₉ gcu	cUGAUgagggccguuaggccGaa	Igaggcu B	10940
1880	UCCAAGC U GUGCCUU	2452	18423	HBV-1880	CHz-7 allyl stabl	a ₉ a ₉ s ₉ g ₉ s ₉ cac	cUGAUgagggccguuaggccGaa	Icuugga B	10941
2382	GAAGAAC U CCCUCGC	2453	18424	HBV-2382	CHz-7 allyl stabl	g ₉ c ₉ s ₉ a ₉ g ₉ ggg	cUGAUgagggccguuaggccGaa	Iuucuuu B	10942
2384	AGAACUC C CUCGCCU	2454	18425	HBV-2384	CHz-7 allyl stabl	a ₉ g ₉ s ₉ c ₉ s ₉ gag	cUGAUgagggccguuaggccGaa	Iaguucu B	10943
2385	GAACUCC C UCGCCUC	2455	18426	HBV-2385	CHz-7 allyl stabl	g ₉ a ₉ s ₉ g ₉ s ₉ cga	cUGAUgagggccguuaggccGaa	Igaguuc B	10944
2422	GCGUGC A GAAGAU	2456	18427	HBV-2422	CHz-7 allyl stabl	g ₉ a ₉ u ₉ s ₉ c ₉ uuc	cUGAUgagggccguuaggccGaa	Icgacgc B	10945
2830	CAUAUUC U UGGGAAC	2457	18428	HBV-2830	CHz-7 allyl stabl	g ₉ u ₉ u ₉ c ₉ s ₉ cca	cUGAUgagggccguuaggccGaa	Iaaauug B	10946
234	AAUCCU C ACAAU	2363	19179	HBV-234	Rz-6 amino stabl	u ₉ a ₉ u ₉ u ₉ s ₉ gu	cUGAUgagggccguuaggccGaa	Aggaau B	10947
252	GAGUCU A GACUCG	2364	19180	HBV-252	Rz-6 amino stabl	c ₉ s ₉ a ₉ g ₉ g ₉ suc	cUGAUgagggccguuaggccGaa	Agacuc B	10948
268	UGGACU U CUCUCA	2365	19182	HBV-268	Rz-6 amino stabl	u ₉ s ₉ a ₉ g ₉ s ₉ gag	cUGAUgagggccguuaggccGaa	Agucca B	10949
280	AAUUU C UAGGGG	2366	19190	HBV-280	Rz-6 amino stabl	c ₉ c ₉ s ₉ c ₉ s ₉ ua	cUGAUgagggccguuaggccGaa	Aaaaau B	10950
313	CAAAAU U CGCAGU	2367	19191	HBV-313	Rz-6 amino stabl	a ₉ c ₉ u ₉ g ₉ s ₉ c ₉ g	cUGAUgagggccguuaggccGaa	Auuuug B	10951
395	GCGGUU U UAUCAU	2368	19195	HBV-395	Rz-6 amino stabl	a ₉ u ₉ s ₉ a ₉ s ₉ ua	cUGAUgagggccguuaggccGaa	Aacgcc B	10952
402	UAUCAU C UUCUCU	2369	19196	HBV-402	Rz-6 amino stabl	g ₉ a ₉ g ₉ g ₉ s ₉ aa	cUGAUgagggccguuaggccGaa	Augaua B	10953
607	UGUAUU C CCAUCC	2370	19200	HBV-607	Rz-6 amino stabl	g ₉ s ₉ a ₉ s ₉ u ₉ gg	cUGAUgagggccguuaggccGaa	Aauaca B	10954
697	UUUGUU C AGUGGU	2371	19207	HBV-697	Rz-6 amino stabl	a ₉ c ₉ s ₉ a ₉ s ₉ cu	cUGAUgagggccguuaggccGaa	Aacaaa B	10955
1539	UCUCUU U ACGCGG	2372	19211	HBV-1539	Rz-6 amino stabl	c ₉ s ₉ a ₉ s ₉ c ₉ s ₉ gu	cUGAUgagggccguuaggccGaa	Aagaga B	10956
1599	UCACCU C UGCACG	2373	19212	HBV-1599	Rz-6 amino stabl	c ₉ g ₉ u ₉ g ₉ s ₉ ca	cUGAUgagggccguuaggccGaa	Agguga B	10957
1607	GCACGU C GCAUGG	2374	19213	HBV-1607	Rz-6 amino stabl	c ₉ s ₉ a ₉ u ₉ s ₉ gc	cUGAUgagggccguuaggccGaa	Acgugc B	10958
1833	UCACCU C UGCCUA	2375	19216	HBV-1833	Rz-6 amino stabl	u ₉ a ₉ g ₉ s ₉ g ₉ ca	cUGAUgagggccguuaggccGaa	Agguga B	10959
2383	AGAACU C CCUCGC	2376	19219	HBV-2383	Rz-6 amino stabl	g ₉ c ₉ a ₉ s ₉ a ₉ gg	cUGAUgagggccguuaggccGaa	Aguucu B	10960
2429	GAAGAU C UCAAUC	2377	19221	HBV-2429	Rz-6 amino stabl	g ₉ a ₉ u ₉ u ₉ ga	cUGAUgagggccguuaggccGaa	Aucuuc B	10961
2831	UAUUCU U GGGAAC	2378	19224	HBV-2831	Rz-6 amino stabl	g ₉ u ₉ u ₉ s ₉ c ₉ cc	cUGAUgagggccguuaggccGaa	Agauua B	10962
430	UGCCUC A UCUCU	2379	19236	HBV-430	CHz-6 amino stabl	a ₉ g ₉ a ₉ a ₉ s ₉ ga	cUGAUgagggccguuaggccGaa	Iaggca B	10963
676	UGGCUC A GUUUAC	2380	19241	HBV-676	CHz-6 amino stabl	g ₉ u ₉ a ₉ s ₉ a ₉ sac	cUGAUgagggccguuaggccGaa	Iagcca B	10964
683	GUUAC U AGUGCC	2381	19242	HBV-683	CHz-6 amino stabl	g ₉ g ₉ c ₉ s ₉ a ₉ s ₉ cu	cUGAUgagggccguuaggccGaa	Iuaaac B	10965

1150	UUUACC C CGUUGC	2382	19247	HBV-1150 CHz-6 amino stabl	G ₅ C ₅ a ₅ s ₅ c ₅ g CUGAUGagggccguuagggccGaa Iguaaa B	10966
1200	GCAACC C CCACUG	2383	19248	HBV-1200 CHz-6 amino stabl	C ₅ a ₅ g ₅ u ₅ g ₅ g CUGAUGagggccguuagggccGaa Iguugc B	10967
1201	CAACCC C CACUGG	2384	19249	HBV-1201 CHz-6 amino stabl	C ₅ s ₅ a ₅ g ₅ u ₅ g CUGAUGagggccguuagggccGaa Igguug B	10968
1444	CGGCGC U GAAUCC	2385	19250	HBV-1444 CHz-6 amino stabl	G ₅ g ₅ a ₅ u ₅ uc CUGAUGagggccguuagggccGaa Icgccg B	10969
1451	GAAUCC C CGGAC	2386	19251	HBV-1451 CHz-6 amino stabl	G ₅ u ₅ C ₅ s ₅ g ₅ c CUGAUGagggccguuagggccGaa Igaauuc B	10970
1533	CGCACC U CUCUUU	2387	19252	HBV-1533 CHz-6 amino stabl	a ₅ s ₅ a ₅ g ₅ s ₅ ag CUGAUGagggccguuagggccGaa Igugcg B	10971
1600	CACCUC U GCACGU	2388	19255	HBV-1600 CHz-6 amino stabl	a ₅ C ₅ g ₅ u ₅ g ₅ c CUGAUGagggccguuagggccGaa Iaggug B	10972
1698	CCGACC U UGAGGC	2389	19256	HBV-1698 CHz-6 amino stabl	G ₅ C ₅ s ₅ u ₅ ca CUGAUGagggccguuagggccGaa Igucgg B	10973
1784	GGAGGC U GUAGGC	2390	19257	HBV-1784 CHz-6 amino stabl	G ₅ C ₅ s ₅ u ₅ ac CUGAUGagggccguuagggccGaa Iccucc B	10974
1829	UUUUUC A CCUCUG	2391	19259	HBV-1829 CHz-6 amino stabl	C ₅ a ₅ g ₅ a ₅ s ₅ g ₅ g CUGAUGagggccguuagggccGaa Iaaaaa B	10975
1876	GCCUCC A AGCUGU	2392	19265	HBV-1876 CHz-6 amino stabl	a ₅ C ₅ g ₅ g ₅ cu CUGAUGagggccguuagggccGaa Igaggc B	10976
1880	CCAAGC U GUGCCU	2393	19267	HBV-1880 CHz-6 amino stabl	a ₅ g ₅ g ₅ C ₅ s ₅ ac CUGAUGagggccguuagggccGaa Icuugg B	10977
218	UUUUUC U GUUGACA	2394	19178	HBV-218 Rz-7 amino stabl	u ₅ g ₅ u ₅ C ₅ s ₅ aac CUGAUGagggccguuagggccGaa Agaaaaa B	10978
257	CUAGACU C GUGGUGG	2395	19181	HBV-257 Rz-7 amino stabl	C ₅ s ₅ a ₅ C ₅ g ₅ cac CUGAUGagggccguuagggccGaa Agucuag B	10979
268	GUGGACU U CUCUCA	2396	19183	HBV-268 Rz-7 amino stabl	u ₅ u ₅ g ₅ a ₅ g ₅ ag CUGAUGagggccguuagggccGaa Aguccac B	10980
269	UGGACUU C UCUCAAU	2397	19184	HBV-269 Rz-7 amino stabl	a ₅ u ₅ u ₅ g ₅ s ₅ aga CUGAUGagggccguuagggccGaa Aagucca B	10981
271	GACUUUC C UCAAUUU	2398	19185	HBV-271 Rz-7 amino stabl	a ₅ s ₅ a ₅ u ₅ s ₅ uga CUGAUGagggccguuagggccGaa Agaaguc B	10982
273	CUUCUCU C AAUUUUC	2399	19186	HBV-273 Rz-7 amino stabl	G ₅ a ₅ a ₅ s ₅ auu CUGAUGagggccguuagggccGaa Agagaag B	10983
277	UCUCAAU U UUCUAGG	2400	19187	HBV-277 Rz-7 amino stabl	C ₅ C ₅ u ₅ a ₅ g ₅ aa CUGAUGagggccguuagggccGaa Auugaga B	10984
278	CUCAAUU U UCUAGGG	2401	19188	HBV-278 Rz-7 amino stabl	C ₅ C ₅ s ₅ u ₅ s ₅ aga CUGAUGagggccguuagggccGaa Auugag B	10985
279	UCAAUUU U CUAGGGG	2402	19189	HBV-279 Rz-7 amino stabl	C ₅ s ₅ C ₅ s ₅ u ₅ ag CUGAUGagggccguuagggccGaa Aaauga B	10986
314	CAAAAUU C GCAGUCC	2403	19192	HBV-314 Rz-7 amino stabl	G ₅ g ₅ a ₅ C ₅ u ₅ gc CUGAUGagggccguuagggccGaa Aauuuug B	10987
385	GAUGUGU C UGCGGCG	2404	19193	HBV-385 Rz-7 amino stabl	C ₅ g ₅ C ₅ s ₅ g ₅ ca CUGAUGagggccguuagggccGaa Acacauc B	10988
394	GCGGCGU U UUAUCAU	2405	19194	HBV-394 Rz-7 amino stabl	a ₅ u ₅ g ₅ a ₅ u ₅ aa CUGAUGagggccguuagggccGaa Acgccgc B	10989
402	UUUAUCAU C UUCCUCU	2406	19197	HBV-402 Rz-7 amino stabl	a ₅ g ₅ s ₅ g ₅ s ₅ g ₅ aa CUGAUGagggccguuagggccGaa Augauaa B	10990
423	UGCUGCU A UGCCUCA	2407	19198	HBV-423 Rz-7 amino stabl	u ₅ g ₅ a ₅ g ₅ g ₅ ca CUGAUGagggccguuagggccGaa Agcagca B	10991
429	UAUGCCU C AUCUUCU	2408	19199	HBV-429 Rz-7 amino stabl	a ₅ g ₅ a ₅ s ₅ g ₅ au CUGAUGagggccguuagggccGaa Aggcaua B	10992
679	GCUCAGU U UACUAGU	2409	19201	HBV-679 Rz-7 amino stabl	a ₅ C ₅ u ₅ s ₅ a ₅ g ₅ ua CUGAUGagggccguuagggccGaa Acugagc B	10993
680	CUCAGUU U ACUAGUG	2410	19202	HBV-680 Rz-7 amino stabl	C ₅ a ₅ s ₅ u ₅ s ₅ agu CUGAUGagggccguuagggccGaa Aacugag B	10994
681	UCAGUUU A CUAGUGC	2411	19203	HBV-681 Rz-7 amino stabl	G ₅ C ₅ a ₅ C ₅ u ₅ ag CUGAUGagggccguuagggccGaa Aaacuga B	10995
684	GUUUACU A GUGCCAU	2412	19204	HBV-684 Rz-7 amino stabl	a ₅ u ₅ g ₅ g ₅ s ₅ cac CUGAUGagggccguuagggccGaa Aguaaac B	10996
692	GUGCCAU U UGUUCAG	2413	19205	HBV-692 Rz-7 amino stabl	C ₅ u ₅ g ₅ a ₅ s ₅ aca CUGAUGagggccguuagggccGaa Auggcac B	10997
693	UGCCAUU U GUUCAGU	2414	19206	HBV-693 Rz-7 amino stabl	a ₅ C ₅ u ₅ g ₅ s ₅ aac CUGAUGagggccguuagggccGaa Aauggca B	10998
1534	CGCACCU C UCUUUAC	2415	19208	HBV-1534 Rz-7 amino stabl	G ₅ u ₅ a ₅ s ₅ aga CUGAUGagggccguuagggccGaa Agguugc B	10999

1536	CACCUCU C UUUACGC	2416	19209	HBV-1536 Rz-7 amino stabl	G ₅ C ₅ G ₅ U ₅ aaa cUGAUGagggccguuaggccGaa Agaggug B	11000
1538	CCUCUCU U UACGGG	2352	19210	HBV-1538 Rz-7 amino stabl	C ₅ C ₅ G ₅ C ₅ gua cUGAUGagggccguuaggccGaa Agagagg B	11001
1787	AGGUCUG A GGCAUAA	2417	19214	HBV-1787 Rz-7 amino stabl	U ₅ U ₅ a ₅ U ₅ gcc cUGAUGagggccguuaggccGaa Acagccu B	11002
1793	UAGGCAU A AAUUGGU	2418	19215	HBV-1793 Rz-7 amino stabl	a ₅ C ₅ C ₅ G ₅ auu cUGAUGagggccguuaggccGaa Augccua B	11003
1874	CAAGCCU C CAAGCUG	2419	19217	HBV-1874 Rz-7 amino stabl	C ₅ a ₅ G ₅ C ₅ uuu cUGAUGagggccguuaggccGaa Aggcuuu B	11004
1887	UGUGCCU U GGGUGGC	2420	19218	HBV-1887 Rz-7 amino stabl	G ₅ C ₅ C ₅ a ₅ ccc cUGAUGagggccguuaggccGaa Aggcaca B	11005
2383	AAGAACU C CCUGGCC	2421	19220	HBV-2383 Rz-7 amino stabl	G ₅ G ₅ C ₅ G ₅ agg cUGAUGagggccguuaggccGaa Aguuuu B	11006
2828	ACCAUAU U CUUGGGA	2422	19222	HBV-2828 Rz-7 amino stabl	U ₅ C ₅ C ₅ G ₅ aag cUGAUGagggccguuaggccGaa Auauugu B	11007
2829	CCAUAUU C UUGGGAA	2423	19223	HBV-2829 Rz-7 amino stabl	U ₅ U ₅ C ₅ C ₅ caa cUGAUGagggccguuaggccGaa Auauagg B	11008
2831	AUAUUUU U GGGAACA	2424	19225	HBV-2831 Rz-7 amino stabl	U ₅ G ₅ U ₅ U ₅ ccc cUGAUGagggccguuaggccGaa Agaauuu B	11009
256	UCUAGAC U CGUGGUG	2425	19226	HBV-256 CHz-7 amino stabl	C ₅ a ₅ C ₅ G ₅ acg cUGAUGagggccguuaggccGaa Iucuaga B	11010
267	GGUGGAC U UCUCUCA	2426	19227	HBV-267 CHz-7 amino stabl	U ₅ G ₅ a ₅ G ₅ aga cUGAUGagggccguuaggccGaa Iuccacc B	11011
270	GGACUUC U CUCAAUU	2427	19228	HBV-270 CHz-7 amino stabl	a ₅ a ₅ U ₅ U ₅ gag cUGAUGagggccguuaggccGaa Iaaguuc B	11012
272	ACUUCUC U CAUUUUU	2428	19229	HBV-272 CHz-7 amino stabl	a ₅ a ₅ a ₅ s ₅ uug cUGAUGagggccguuaggccGaa Iagaagu B	11013
274	UUCUCUC A AUUUUCU	2429	19230	HBV-274 CHz-7 amino stabl	a ₅ g ₅ a ₅ s ₅ aau cUGAUGagggccguuaggccGaa Iagagaa B	11014
386	AUGUGUC U GCGGGCU	2430	19231	HBV-386 CHz-7 amino stabl	a ₅ C ₅ G ₅ C ₅ cg cUGAUGagggccguuaggccGaa Iacacau B	11015
419	AUCCUGC U GCUAUGC	2431	19232	HBV-419 CHz-7 amino stabl	G ₅ C ₅ a ₅ U ₅ agc cUGAUGagggccguuaggccGaa Icaggau B	11016
422	CUGCUGC U AUGCCUC	2432	19233	HBV-422 CHz-7 amino stabl	G ₅ a ₅ G ₅ G ₅ cau cUGAUGagggccguuaggccGaa Icagcag B	11017
427	GUUAUGC C UCAUCUU	2433	19234	HBV-427 CHz-7 amino stabl	a ₅ a ₅ G ₅ a ₅ uga cUGAUGagggccguuaggccGaa Icauagc B	11018
428	CUAUGCC U CAUCUUC	2434	19235	HBV-428 CHz-7 amino stabl	G ₅ a ₅ a ₅ G ₅ aug cUGAUGagggccguuaggccGaa Igcauag B	11019
430	AUGCCUC A UCUCUUU	2435	19237	HBV-430 CHz-7 amino stabl	a ₅ a ₅ G ₅ a ₅ aga cUGAUGagggccguuaggccGaa Iaggcau B	11020
608	UGUAUUC C CAUCCCA	2436	19238	HBV-608 CHz-7 amino stabl	U ₅ G ₅ G ₅ G ₅ aug cUGAUGagggccguuaggccGaa Iaaauaca B	11021
609	GUUAUCC C AUCCCAU	2437	19239	HBV-609 CHz-7 amino stabl	a ₅ U ₅ G ₅ G ₅ gau cUGAUGagggccguuaggccGaa Igaauac B	11022
669	GUUUCUC U UGGCUCA	2438	19240	HBV-669 CHz-7 amino stabl	U ₅ G ₅ a ₅ G ₅ cca cUGAUGagggccguuaggccGaa Iagaaac B	11023
689	CUAGUGC C AUUUGUU	2439	19243	HBV-689 CHz-7 amino stabl	a ₅ a ₅ C ₅ a ₅ aa cUGAUGagggccguuaggccGaa Icacuag B	11024
690	UAGUGCC A UUUGUUC	2440	19244	HBV-690 CHz-7 amino stabl	G ₅ a ₅ a ₅ C ₅ aaa cUGAUGagggccguuaggccGaa Igcacua B	11025
718	GUUUUCC C CCACUGU	2441	19245	HBV-718 CHz-7 amino stabl	a ₅ C ₅ a ₅ G ₅ ugg cUGAUGagggccguuaggccGaa Igaaagc B	11026
1149	CCUUUAC C CCGUUGC	2442	19246	HBV-1149 CHz-7 amino stabl	G ₅ C ₅ a ₅ s ₅ cg cUGAUGagggccguuaggccGaa Iuaaagg B	11027
1535	GCACCUC U CUUUACG	2443	19253	HBV-1535 CHz-7 amino stabl	C ₅ G ₅ U ₅ a ₅ aa cUGAUGagggccguuaggccGaa Iaggugc B	11028
1537	ACCUCUC U UUACGGG	2444	19254	HBV-1537 CHz-7 amino stabl	C ₅ G ₅ C ₅ G ₅ uaa cUGAUGagggccguuaggccGaa Iagaggu B	11029
1791	UGUAGGC A UAAAUUG	2445	19258	HBV-1791 CHz-7 amino stabl	C ₅ a ₅ a ₅ U ₅ uaa cUGAUGagggccguuaggccGaa Iccuaca B	11030
1831	UUUUCAC C UCUGCCU	2446	19260	HBV-1831 CHz-7 amino stabl	a ₅ G ₅ G ₅ C ₅ aga cUGAUGagggccguuaggccGaa Iugaaaa B	11031
1832	UUUACCC U CUGCCUA	2447	19261	HBV-1832 CHz-7 amino stabl	U ₅ a ₅ G ₅ G ₅ cag cUGAUGagggccguuaggccGaa Igugaaa B	11032
1872	UUCAAGC C UCCAAGC	2448	19262	HBV-1872 CHz-7 amino stabl	G ₅ C ₅ U ₅ U ₅ gga cUGAUGagggccguuaggccGaa Icuugaa B	11033

1873	UCAAGCC U CCAAGCU	2449	19263	HBV-1873	CHz-7	amino	stabi	a ₉ g ₉ c ₉ u ₉ ugg	cUGAU/GagggccguuaggccGaa	IgcuuGa	B	11034		
1875	AAGCCUC C AAGCUGU	2450	19264	HBV-1875	CHz-7	amino	stabi	a ₉ s ₉ a ₉ g ₉ s ₉ cuu	cUGAU/GagggccguuaggccGaa	Iagggcuu	B	11035		
1876	AGCCUCC A AGCUGUG	2451	19266	HBV-1876	CHz-7	amino	stabi	c ₉ a ₉ s ₉ a ₉ g ₉ cu	cUGAU/GagggccguuaggccGaa	Igagggcu	B	11036		
1880	UCCAAGC U GUGCCUU	2452	19268	HBV-1880	CHz-7	amino	stabi	a ₉ s ₉ g ₉ s ₉ g ₉ cac	cUGAU/GagggccguuaggccGaa	Icuugga	B	11037		
2382	GAAGAAC U CCUCUGC	2453	19269	HBV-2382	CHz-7	amino	stabi	g ₉ s ₉ g ₉ s ₉ a ₉ ggg	cUGAU/GagggccguuaggccGaa	Iuuuuc	B	11038		
2384	AGAACUC C CUCGCCU	2454	19270	HBV-2384	CHz-7	amino	stabi	a ₉ g ₉ g ₉ s ₉ c ₉ gag	cUGAU/GagggccguuaggccGaa	Iaguucu	B	11039		
2385	GAACUCC C UCGCCUC	2455	19271	HBV-2385	CHz-7	amino	stabi	g ₉ s ₉ g ₉ s ₉ g ₉ cga	cUGAU/GagggccguuaggccGaa	Igaguuc	B	11040		
2422	CGCUGCG A GAAGAU	2456	19272	HBV-2422	CHz-7	amino	stabi	g ₉ s ₉ u ₉ s ₉ c ₉ cca	cUGAU/GagggccguuaggccGaa	Igcagcg	B	11041		
2830	CAUAUUC U UGGGAAC	2457	19273	HBV-2830	CHz-7	amino	stabi	g ₉ u ₉ u ₉ s ₉ c ₉ cca	cUGAU/GagggccguuaggccGaa	Iaauaug	B	11042		
315	GCCAAAUAUC G CAGUC	2458	20079	HBV-315	GCL.Rz-5/10	stab2		g ₉ a ₉ s ₉ c ₉ g	uGAU ₉ g	gcaUGcacuau	gcg	gaaunuugcg	B	11043
381	AUCGCUGGAU G UGUUCU	2459	20080	HBV-381	GCL.Rz-5/10	stab2		a ₉ g ₉ a ₉ a	uGAU ₉ g	gcaUGcacuau	gcg	auccagcgau	B	11044
476	UUGCCCGUUU G UCCUC	2460	20081	HBV-476	GCL.Rz-5/10	stab2		g ₉ a ₉ g ₉ a	uGAU ₉ g	gcaUGcacuau	gcg	aaacgggcaa	B	11045
694	AGUGCCAUUU G UUCAG	2461	20082	HBV-694	GCL.Rz-5/10	stab2		c ₉ u ₉ g ₉ a	uGAU ₉ g	gcaUGcacuau	gcg	aaauuggcacu	B	11046
1265	CUCCUCUGCC G AUCCA	2462	20083	HBV-1265	GCL.Rz-5/10	stab2		u ₉ g ₉ g ₉ u	uGAU ₉ g	gcaUGcacuau	gcg	ggcagaggag	B	11047
1601	CUUCACCUUC G CACGU	2463	20084	HBV-1601	GCL.Rz-5/10	stab2		a ₉ s ₉ g ₉ g	uGAU ₉ g	gcaUGcacuau	gcg	agaggugaag	B	11048
1881	CUUCCAAGCU G UGCCU	2464	20085	HBV-1881	GCL.Rz-5/10	stab2		a ₉ g ₉ g ₉ a	uGAU ₉ g	gcaUGcacuau	gcg	agcuuggagg	B	11049
1883	UCCAAGCUGU G CCUUG	2465	20086	HBV-1883	GCL.Rz-5/10	stab2		c ₉ a ₉ s ₉ g	uGAU ₉ g	gcaUGcacuau	gcg	acagcuugga	B	11050
2388	GAACUCCUC G CCUCG	2466	20087	HBV-2388	GCL.Rz-5/10	stab2		c ₉ g ₉ s ₉ g	uGAU ₉ g	gcaUGcacuau	gcg	gagggaguuc	B	11051
381	GCUGGAU G UGUCUGC	2467	20091	HBV-381	Zin.Rz-7	amino	stab2	g ₉ s ₉ a ₉ g ₉ s ₉ aca	GcgaaagGCGaGugaGGuCu	auccagc	B		11052	
392	CUGCGGC G UUUUAUC	2468	20092	HBV-392	Zin.Rz-7	amino	stab2	g ₉ a ₉ u ₉ a ₉ aaa	GcgaaagGCGaGugaGGuCu	gccgcag	B		11053	
420	UCCUGCU G CUAUGCC	2469	20093	HBV-420	Zin.Rz-7	amino	stab2	g ₉ s ₉ c ₉ s ₉ a ₉ uag	GccgaaagGCGaGugaGGuCu	agcagga	B		11054	
648	UAUGGGA G UGGGCCU	2470	20094	HBV-648	Zin.Rz-7	amino	stab2	a ₉ g ₉ g ₉ c ₉ cca	GcgaaagGCGaGugaGGuCu	ucccaua	B		11055	
711	UCGUAGG G CUUCCCC	2471	20095	HBV-711	Zin.Rz-7	amino	stab2	g ₉ g ₉ s ₉ a ₉ s ₉ aaag	GccgaaagGCGaGugaGGuCu	ccuacga	B		11056	
1262	CUCCUCU G CCGAUCC	2472	20096	HBV-1262	Zin.Rz-7	amino	stab2	g ₉ g ₉ a ₉ u ₉ s ₉ cgg	GccgaaagGCGaGugaGGuCu	agaggag	B		11057	
1835	CACCUUC G CCUAUUC	2473	20097	HBV-1835	Zin.Rz-7	amino	stab2	g ₉ a ₉ u ₉ s ₉ agg	GccgaaagGCGaGugaGGuCu	agaaggug	B		11058	
2388	CUCCUC G CCUCGCA	2474	20098	HBV-2388	Zin.Rz-7	amino	stab2	u ₉ g ₉ c ₉ g ₉ agg	GccgaaagGCGaGugaGGuCu	gagggag	B		11059	
192	GACCCCU G CUCUGU	2475	20099	HBV-192	Zin.Rz-7	amino	stab2	a ₉ s ₉ a ₉ s ₉ c ₉ gag	GccgaaagGCGaGugaGGuCu	agggguc	B		11060	
198	UGCUCGU G UUAACAG	2476	20100	HBV-198	Zin.Rz-7	amino	stab2	c ₉ s ₉ u ₉ g ₉ uaa	GccgaaagGCGaGugaGGuCu	acgagca	B		11061	

315	AAAAUUC G CAGUCCC	2477	20101	HBV-315 Zin.Rz-7 stab2	amino	gsgsgsa ₃ cug GccgaaagCCGaGugaGGuCu gaauuuu B	11062
383	GGAUGU G UCUGCG	2478	20102	HBV-383 Zin.Rz-6 stab2	amino	csgscsa ₃ ga GccgaaagCCGaGugaGGuCu acaucc B	11063
383	UGGAUGU G UCUGCGG	2479	20103	HBV-383 Zin.Rz-7 stab2	amino	csgscsa ₃ aga GccgaaagCCGaGugaGGuCu acaucca B	11064
387	GUGUCU G CGGCGU	2480	20104	HBV-387 Zin.Rz-6 stab2	amino	ascs ₃ gsc ₃ cg GccgaaagCCGaGugaGGuCu agacac B	11065
390	GUCUGCG G CGUUUUA	2481	20105	HBV-390 Zin.Rz-7 stab2	amino	us ₃ a ₃ sa ₃ acg GccgaaagCCGaGugaGGuCu cgcagac B	11066
392	UGCUGC G UUUUAU	2482	20106	HBV-392 Zin.Rz-6 stab2	amino	as ₃ sa ₃ sa ₃ aa GccgaaagCCGaGugaGGuCu gccgca B	11067
425	UGCUAU G CCUCAU	2483	20107	HBV-425 Zin.Rz-6 stab2	amino	as ₃ us ₃ sa ₃ gg GccgaaagCCGaGugaGGuCu auagca B	11068
425	CUGCUAU G CCUCAUC	2484	20108	HBV-425 Zin.Rz-7 stab2	amino	gsgsa ₃ us ₃ gsgg GccgaaagCCGaGugaGGuCu auagcag B	11069
468	GUAUGUU G CCCGUUU	2485	20109	HBV-468 Zin.Rz-7 stab2	amino	as ₃ a ₃ sa ₃ csggg GccgaaagCCGaGugaGGuCu aacauac B	11070
476	CCCGUUU G UCCUCUA	2486	20110	HBV-476 Zin.Rz-7 stab2	amino	us ₃ as ₃ gsgsa ₃ gga GccgaaagCCGaGugaGGuCu aaacggg B	11071
648	AUGGGA G UGGGCC	2487	20111	HBV-648 Zin.Rz-6 stab2	amino	gsgscsa ₃ c ₃ ca GccgaaagCCGaGugaGGuCu uccau B	11072
694	GCCAUUU G UUCAGUG	2488	20112	HBV-694 Zin.Rz-7 stab2	amino	csgsa ₃ c ₃ us ₃ gaa GccgaaagCCGaGugaGGuCu aaauagg B	11073
699	UUGUUCA G UGGUUCG	2489	20113	HBV-699 Zin.Rz-7 stab2	amino	csgsa ₃ sa ₃ c ₃ ca GccgaaagCCGaGugaGGuCu ugaacaa B	11074
1262	UCCUCU G CCGAUC	2490	20114	HBV-1262 Zin.Rz-6 stab2	amino	gsgsa ₃ us ₃ c ₃ gg GccgaaagCCGaGugaGGuCu agagga B	11075
1440	CCCGUCG G CGCUGAA	2491	20115	HBV-1440 Zin.Rz-7 stab2	amino	us ₃ us ₃ c ₃ sa ₃ g ₃ cg GccgaaagCCGaGugaGGuCu cgacggg B	11076
1526	CACGGG G CGCACC	2492	20116	HBV-1526 Zin.Rz-6 stab2	amino	gsgsa ₃ us ₃ g ₃ cg GccgaaagCCGaGugaGGuCu cccgug B	11077
1526	CCACGGG G CGCACCU	2493	20117	HBV-1526 Zin.Rz-7 stab2	amino	as ₃ gsgsa ₃ us ₃ g ₃ cg GccgaaagCCGaGugaGGuCu cccgugg B	11078
1557	CCCGUCU G UGCCUUC	2494	20118	HBV-1557 Zin.Rz-7 stab2	amino	gsgsa ₃ a ₃ gsgca GccgaaagCCGaGugaGGuCu agacggg B	11079
1559	CGUCUGU G CCUUCUC	2495	20119	HBV-1559 Zin.Rz-7 stab2	amino	gsgsa ₃ gsgsa ₃ g ₃ gg GccgaaagCCGaGugaGGuCu acagacg B	11080
1590	GCACUUC G CUUCACC	2496	20120	HBV-1590 Zin.Rz-7 stab2	amino	gsgsa ₃ us ₃ g ₃ aag GccgaaagCCGaGugaGGuCu gaagugc B	11081
1835	ACCUCU G CCUAAU	2497	20121	HBV-1835 Zin.Rz-6 stab2	amino	as ₃ us ₃ us ₃ a ₃ ggg GccgaaagCCGaGugaGGuCu agaggu B	11082
2311	ACCAAAU G CCCCUAU	2498	20122	HBV-2311 Zin.Rz-7 stab2	amino	as ₃ us ₃ as ₃ gsggg GccgaaagCCGaGugaGGuCu auuuggu B	11083

2420	CCGCGUC G CAGAAGA	2499	20123	HBV-2420 Zin.Rz-7 stab2	amino	u ₃ c ₈ a ₃ u ₃ u ₃ cug GccgaaaagCCGaGugaGGuCu	gacgcgg B	11084
65	CTUGCUG G UGGCUCC	2500	20124	HBV-65 Zin.Rz-7 stab2	amino	g ₃ g ₃ a ₃ g ₃ cca GccgaaaagCCGaGugaGGuCu	cagcagg B	11085
192	ACCCCU G CUCGUG	2501	20125	HBV-192 Zin.Rz-6 stab2	amino	c ₃ a ₃ c ₃ g ₃ ag GccgaaaagCCGaGugaGGuCu	aggggu B	11086
198	GCUCGU G UUACAG	2502	20126	HBV-198 Zin.Rz-6 stab2	amino	c ₃ u ₃ g ₃ u ₃ aa GccgaaaagCCGaGugaGGuCu	acgagc B	11087
258	UAGACUC G UGGUGGA	2503	20127	HBV-258 Zin.Rz-7 stab2	amino	u ₃ c ₃ c ₃ a ₃ cca GccgaaaagCCGaGugaGGuCu	gagucua B	11088
261	ACUCGUG G UGGACUU	2504	20128	HBV-261 Zin.Rz-7 stab2	amino	a ₃ a ₃ g ₃ u ₃ cca GccgaaaagCCGaGugaGGuCu	cacgagu B	11089
315	AAAUUC G CAGUCC	2505	20129	HBV-315 Zin.Rz-6 stab2	amino	g ₃ g ₃ a ₃ c ₃ ug GccgaaaagCCGaGugaGGuCu	gaauuu B	11090
381	CUGGAU G UGUCUG	2506	20130	HBV-381 Zin.Rz-6 stab2	amino	c ₃ a ₃ g ₃ a ₃ ca GccgaaaagCCGaGugaGGuCu	auccag B	11091
387	UGUGUCU G CGGCGUU	2507	20131	HBV-387 Zin.Rz-7 stab2	amino	a ₃ a ₃ c ₃ g ₃ ccg GccgaaaagCCGaGugaGGuCu	agacaca B	11092
390	UCUGCG G CGUUUU	2508	20132	HBV-390 Zin.Rz-6 stab2	amino	a ₃ a ₃ a ₃ a ₃ c ₃ g GccgaaaagCCGaGugaGGuCu	cgcaga B	11093
417	CAUCCU G CUGCUA	2509	20133	HBV-417 Zin.Rz-6 stab2	amino	u ₃ a ₃ g ₃ c ₃ ag GccgaaaagCCGaGugaGGuCu	aggau B	11094
420	CCUGCU G CUAUGC	2510	20134	HBV-420 Zin.Rz-6 stab2	amino	g ₃ c ₃ a ₃ u ₃ ag GccgaaaagCCGaGugaGGuCu	agcagg B	11095
468	UAUGU G CCCGUU	2511	20135	HBV-468 Zin.Rz-6 stab2	amino	a ₃ a ₃ c ₃ g ₃ gg GccgaaaagCCGaGugaGGuCu	aacaua B	11096
476	CCGUUU G UCCUCU	2512	20136	HBV-476 Zin.Rz-6 stab2	amino	a ₃ g ₃ a ₃ g ₃ ga GccgaaaagCCGaGugaGGuCu	aaacgg B	11097
677	GGCUCA G UUUACU	2513	20137	HBV-677 Zin.Rz-6 stab2	amino	a ₃ g ₃ u ₃ a ₃ aa GccgaaaagCCGaGugaGGuCu	ugagcc B	11098
677	UGGCUCA G UUUACUA	2514	20138	HBV-677 Zin.Rz-7 stab2	amino	u ₃ a ₃ g ₃ u ₃ aaa GccgaaaagCCGaGugaGGuCu	ugagcca B	11099
685	UUACUA G UGCCAU	2515	20139	HBV-685 Zin.Rz-6 stab2	amino	a ₃ u ₃ g ₃ g ₃ ca GccgaaaagCCGaGugaGGuCu	uaguaa B	11100
685	UUUACUA G UGCCAUU	2516	20140	HBV-685 Zin.Rz-7 stab2	amino	a ₃ a ₃ u ₃ g ₃ gca GccgaaaagCCGaGugaGGuCu	uaguaaa B	11101
687	UACUAGU G CCAUUUG	2517	20141	HBV-687 Zin.Rz-7 stab2	amino	c ₃ a ₃ a ₃ a ₃ ugg GccgaaaagCCGaGugaGGuCu	acuagua B	11102
699	UGUUCA G UGGUUC	2518	20142	HBV-699 Zin.Rz-6 stab2	amino	g ₃ a ₃ a ₃ c ₃ ca GccgaaaagCCGaGugaGGuCu	ugaaca B	11103
702	UCAGUG G UUCGUA	2519	20143	HBV-702 Zin.Rz-6 stab2	amino	u ₃ a ₃ c ₃ g ₃ aa GccgaaaagCCGaGugaGGuCu	cacuga B	11104
702	UUCAGUG G UUCGUAG	2520	20144	HBV-702 Zin.Rz-7 stab2	amino	c ₃ u ₃ a ₃ c ₃ gaa GccgaaaagCCGaGugaGGuCu	cacugaa B	11105

711	CGUAGG G CUUUC	2521	20145	HBV-711 Zin.Rz-6 stab2	amino	g ₅ g ₅ a ₅ a ₅ ag GccgaaagCGGaGugaGGuCu ccuacg B	11106
1006	UUGUGG G UCUUUU	2522	20146	HBV-1006 Zin.Rz-6 stab2	amino	a ₅ a ₅ a ₅ a ₅ ga GccgaaagCGGaGugaGGuCu ccacaa B	11107
1103	UUUCUC G CCAACU	2523	20147	HBV-1103 Zin.Rz-6 stab2	amino	a ₅ g ₅ u ₅ u ₅ gg GccgaaagCGGaGugaGGuCu gagaaa B	11108
1103	CUUUCUC G CCAACUU	2524	20148	HBV-1103 Zin.Rz-7 stab2	amino	a ₅ a ₅ g ₅ u ₅ u ₅ gg GccgaaagCGGaGugaGGuCu gagaaa B	11109
1184	GCCAAGU G UUUGCUG	2525	20149	HBV-1184 Zin.Rz-7 stab2	amino	c ₅ a ₅ g ₅ c ₅ aaa GccgaaagCGGaGugaGGuCu acuuggc B	11110
1440	CCGUCG G CGCUGA	2526	20150	HBV-1440 Zin.Rz-6 stab2	amino	u ₅ c ₅ a ₅ g ₅ c ₅ g GccgaaagCGGaGugaGGuCu cgacgg B	11111
1442	GUCGGC G CUGAAU	2527	20151	HBV-1442 Zin.Rz-6 stab2	amino	a ₅ u ₅ u ₅ c ₅ ag GccgaaagCGGaGugaGGuCu gccgac B	11112
1442	CGUCGGC G CUGAAUC	2528	20152	HBV-1442 Zin.Rz-7 stab2	amino	g ₅ a ₅ u ₅ u ₅ cag GccgaaagCGGaGugaGGuCu gccgacg B	11113
1553	CUCCCC G UCUGUG	2529	20153	HBV-1553 Zin.Rz-6 stab2	amino	c ₅ a ₅ c ₅ a ₅ ga GccgaaagCGGaGugaGGuCu ggggag B	11114
1557	CCGUCU G UGCCUU	2530	20154	HBV-1557 Zin.Rz-6 stab2	amino	a ₅ a ₅ g ₅ g ₅ ca GccgaaagCGGaGugaGGuCu agacgg B	11115
1559	GUCUGU G CCUUCU	2531	20155	HBV-1559 Zin.Rz-6 stab2	amino	a ₅ g ₅ a ₅ a ₅ ggg GccgaaagCGGaGugaGGuCu acagac B	11116
1583	CCGUGU G CACUUC	2532	20156	HBV-1583 Zin.Rz-6 stab2	amino	g ₅ a ₅ a ₅ g ₅ ug GccgaaagCGGaGugaGGuCu acacgg B	11117
1590	CACUUC G CUUCAC	2533	20157	HBV-1590 Zin.Rz-6 stab2	amino	g ₅ u ₅ g ₅ a ₅ ag GccgaaagCGGaGugaGGuCu gaagug B	11118
1622	ACCACC G UGAACG	2534	20158	HBV-1622 Zin.Rz-6 stab2	amino	c ₅ g ₅ u ₅ u ₅ ca GccgaaagCGGaGugaGGuCu gguggu B	11119
1870	UGUUCAA G CCUCCAA	2535	20159	HBV-1870 Zin.Rz-7 stab2	amino	u ₅ u ₅ g ₅ g ₅ ggg GccgaaagCGGaGugaGGuCu uugaaca B	11120
1881	CCAAGCU G UGCCUUG	2536	20160	HBV-1881 Zin.Rz-7 stab2	amino	c ₅ a ₅ a ₅ g ₅ gca GccgaaagCGGaGugaGGuCu agcuugg B	11121
1883	AGCUGU G CCUUGG	2537	20161	HBV-1883 Zin.Rz-6 stab2	amino	c ₅ c ₅ a ₅ a ₅ ggg GccgaaagCGGaGugaGGuCu acagcu B	11122
1883	AAGCUGU G CCUUGGG	2538	20162	HBV-1883 Zin.Rz-7 stab2	amino	c ₅ c ₅ c ₅ a ₅ ggg GccgaaagCGGaGugaGGuCu acagcuu B	11123
2311	CCAAAU G CCCCUA	2539	20163	HBV-2311 Zin.Rz-6 stab2	amino	u ₅ a ₅ g ₅ g ₅ gg GccgaaagCGGaGugaGGuCu auuugg B	11124
2347	ACUGUU G UUAGAC	2540	20164	HBV-2347 Zin.Rz-6 stab2	amino	g ₅ u ₅ c ₅ u ₅ aa GccgaaagCGGaGugaGGuCu aacagu B	11125
2364	AGGCAG G UCCCCU	2541	20165	HBV-2364 Zin.Rz-6 stab2	amino	a ₅ g ₅ g ₅ g ₅ ga GccgaaagCGGaGugaGGuCu cugccu B	11126
2364	GAGGCAG G UCCCCUA	2542	20166	HBV-2364 Zin.Rz-7 stab2	amino	u ₅ a ₅ g ₅ g ₅ gga GccgaaagCGGaGugaGGuCu cugccuc B	11127

2388	UCCUC G CCUCG	2543	20167	HBV-2388 Zin.Rz-6 amino stab2	G ₅ C ₅ G ₅ a ₅ gg GccgaaagcGgGugaGGuCu gagggg B	11128
2393	CGCCUC G CAGACG	2544	20168	HBV-2393 Zin.Rz-6 amino stab2	C ₅ G ₅ u ₅ C ₅ ug GccgaaagcGgGugaGGuCu gagggc B	11129
2417	CGCCGC G UCGCAG	2545	20169	HBV-2417 Zin.Rz-6 amino stab2	C ₅ u ₅ G ₅ C ₅ ga GccgaaagcGgGugaGGuCu gcggcg B	11130
2420	CGCGUC G CAGAAG	2546	20170	HBV-2420 Zin.Rz-6 amino stab2	C ₅ u ₅ u ₅ C ₅ ug GccgaaagcGgGugaGGuCu gacgcg B	11131
2474	CAUAAG G UGGGAA	2547	20171	HBV-2474 Zin.Rz-6 amino stab2	u ₅ u ₅ C ₅ C ₅ ca GccgaaagcGgGugaGGuCu cuuaug B	11132
381	GCUGAU G UGUCUG	2467	20172	HBV-381 Amb.Rz-7 stab2	G ₅ C ₅ a ₅ G ₅ aca gga L ucCCUUCaagga L ucCGGG auccagc B	11133
648	UAUGGA G UGGGCCU	2470	20173	HBV-648 Amb.Rz-7 stab2	a ₅ G ₅ G ₅ C ₅ cca gga L ucCCUUCaagga L ucCGGG ucccaua B	11134
198	UGCUCGU G UUACAGG	2476	20174	HBV-198 Amb.Rz-7 stab2	C ₅ C ₅ u ₅ G ₅ uaa gga L ucCCUUCaagga L ucCGGG acgagca B	11135
377	UAUCGU G GAUGUGU	2548	20175	HBV-377 Amb.Rz-7 stab2	a ₅ C ₅ a ₅ C ₅ auc gga L ucCCUUCaagga L ucCGGG agcgaua B	11136
378	AUCGUG G AUGUGUC	2549	20176	HBV-378 Amb.Rz-7 stab2	G ₅ a ₅ C ₅ a ₅ cau gga L ucCCUUCaagga L ucCGGG cagcgau B	11137
383	UGGAUGU G UCUGCGG	2479	20177	HBV-383 Amb.Rz-7 stab2	C ₅ C ₅ G ₅ C ₅ aga gga L ucCCUUCaagga L ucCGGG acaucca B	11138
383	GGAUGU G UCUGCG	2478	20178	HBV-383 Amb.Rz-6 stab2	C ₅ G ₅ C ₅ a ₅ ga gga L ucCCUUCaagga L ucCGGG acaucc B	11139
648	AUGGA G UGGGCC	2487	20179	HBV-648 Amb.Rz-6 stab2	G ₅ G ₅ C ₅ C ₅ ca gga L ucCCUUCaagga L ucCGGG ucccau B	11140
650	UGGAGU G GGCCUCA	2550	20180	HBV-650 Amb.Rz-7 stab2	u ₅ G ₅ a ₅ G ₅ gcc gga L ucCCUUCaagga L ucCGGG acucca B	11141
650	GGGAGU G GGCCUC	2551	20181	HBV-650 Amb.Rz-6 stab2	G ₅ a ₅ G ₅ G ₅ cc gga L ucCCUUCaagga L ucCGGG acucc B	11142
694	GCCAUUU G UUCAGUG	2488	20182	HBV-694 Amb.Rz-7 stab2	C ₅ a ₅ C ₅ u ₅ gaa gga L ucCCUUCaagga L ucCGGG aauggc B	11143
699	UUGUUA G UGGUUG	2489	20183	HBV-699 Amb.Rz-7 stab2	C ₅ G ₅ a ₅ C ₅ cca gga L ucCCUUCaagga L ucCGGG ugaacaa B	11144
701	GUUCAGU G GUUCGUA	2552	20184	HBV-701 Amb.Rz-7 stab2	u ₅ a ₅ C ₅ G ₅ aac gga L ucCCUUCaagga L ucCGGG acugaac B	11145
710	UUCGUAG G GCUUUC	2553	20185	HBV-710 Amb.Rz-7 stab2	G ₅ G ₅ a ₅ a ₅ agc gga L ucCCUUCaagga L ucCGGG cuacgaa B	11146
1525	CCACGG G GCGCAC	2554	20186	HBV-1525 Amb.Rz-6 stab2	G ₅ u ₅ G ₅ C ₅ gc gga L ucCCUUCaagga L ucCGGG ccgugg B	11147
1624	CACCGU G AACGCC	2555	20187	HBV-1624 Amb.Rz-6 stab2	G ₅ G ₅ C ₅ G ₅ uu gga L ucCCUUCaagga L ucCGGG acggug B	11148
2069	CACUCA G GCAAGC	2556	20188	HBV-2069 Amb.Rz-6 stab2	G ₅ C ₅ u ₅ u ₅ gc gga L ucCCUUCaagga L ucCGGG ugagug B	11149
2375	CCUAGAA G AAGAACU	2557	20189	HBV-2375 Amb.Rz-7 stab2	a ₅ G ₅ u ₅ u ₅ cuu gga L ucCCUUCaagga L ucCGGG uuucua B	11150
2476	AUAAGGU G GGAACU	2558	20190	HBV-2476 Amb.Rz-7 stab2	a ₅ G ₅ u ₅ u ₅ ucc gga L ucCCUUCaagga L ucCGGG accuuau B	11151
65	CCUGCUG G UGGUCC	2500	20191	HBV-65 Amb.Rz-7 stab2	G ₅ G ₅ a ₅ G ₅ cca gga L ucCCUUCaagga L ucCGGG cagcagg B	11152
67	GCUGGU G GCUCCA	2559	20192	HBV-67 Amb.Rz-6 stab2	u ₅ G ₅ G ₅ a ₅ gc gga L ucCCUUCaagga L ucCGGG accagc B	11153
198	GCUCGU G UUACAG	2502	20193	HBV-198 Amb.Rz-6 stab2	C ₅ u ₅ G ₅ u ₅ aa gga L ucCCUUCaagga L ucCGGG acgagc B	11154
260	GACUGU G GUGGACU	2560	20194	HBV-260 Amb.Rz-7 stab2	a ₅ G ₅ u ₅ C ₅ cac gga L ucCCUUCaagga L ucCGGG acgaguc B	11155
263	UCGUGGU G GACUUCU	2561	20195	HBV-263 Amb.Rz-7 stab2	a ₅ G ₅ a ₅ G ₅ guc gga L ucCCUUCaagga L ucCGGG accacga B	11156
377	AUCGCU G GAUGUG	2562	20196	HBV-377 Amb.Rz-6 stab2	C ₅ a ₅ C ₅ a ₅ uc gga L ucCCUUCaagga L ucCGGG agcgau B	11157
378	UCGCGU G AUGUGU	2563	20197	HBV-378 Amb.Rz-6 stab2	a ₅ C ₅ a ₅ C ₅ au gga L ucCCUUCaagga L ucCGGG cagcga B	11158

476	CCGUUU G UCCUCU	2512	20198	HBV-476 Amb.Rz-6 stab2	a ₉ g ₉ a ₉ g ₉ g ₉ gga L ucCCUUCaagga L ucCGGG aaacgg B	11159
651	GGGAGUG G GCCUCAG	2564	20199	HBV-651 Amb.Rz-7 stab2	c ₉ u ₉ g ₉ a ₉ g ₉ g ₉ c gga L ucCCUUCaagga L ucCGGG cacuccc B	11160
677	UGGCUCA G UUUACUA	2514	20200	HBV-677 Amb.Rz-7 stab2	u ₉ a ₉ g ₉ u ₉ g ₉ aaa gga L ucCCUUCaagga L ucCGGG ugagcca B	11161
685	UUUACUA G UGCCAUU	2516	20201	HBV-685 Amb.Rz-7 stab2	a ₉ a ₉ u ₉ g ₉ g ₉ c gga L ucCCUUCaagga L ucCGGG uaguaaa B	11162
702	UUCAGUG G UUCGUAG	2520	20202	HBV-702 Amb.Rz-7 stab2	c ₉ u ₉ a ₉ c ₉ g ₉ g ₉ gga L ucCCUUCaagga L ucCGGG cacugaa B	11163
709	GUUCGUA G GGCUUUC	2565	20203	HBV-709 Amb.Rz-7 stab2	g ₉ a ₉ a ₉ a ₉ g ₉ g ₉ c gga L ucCCUUCaagga L ucCGGG uacgaac B	11164
710	UCGVAG G GCUUUC	2566	20204	HBV-710 Amb.Rz-6 stab2	g ₉ a ₉ a ₉ a ₉ g ₉ c gga L ucCCUUCaagga L ucCGGG cuacga B	11165
747	UAUGGAU G AUGUGGU	2567	20205	HBV-747 Amb.Rz-7 stab2	a ₉ c ₉ c ₉ a ₉ g ₉ cau gga L ucCCUUCaagga L ucCGGG auccaau B	11166
1557	CCGUUU G UGCCUU	2530	20206	HBV-1557 Amb.Rz-6 stab2	a ₉ a ₉ g ₉ g ₉ c gga L ucCCUUCaagga L ucCGGG agacgg B	11167
1881	CCAAGCU G UGCCUUG	2536	20207	HBV-1881 Amb.Rz-7 stab2	c ₉ a ₉ a ₉ g ₉ g ₉ c gga L ucCCUUCaagga L ucCGGG agcuugg B	11168
2347	ACUGUU G UUAGAC	2540	20208	HBV-2347 Amb.Rz-6 stab2	g ₉ u ₉ c ₉ u ₉ g ₉ aa gga L ucCCUUCaagga L ucCGGG aacagu B	11169
2375	CUAGAA G AAGAAC	2568	20209	HBV-2375 Amb.Rz-6 stab2	g ₉ u ₉ u ₉ c ₉ uu gga L ucCCUUCaagga L ucCGGG uucuag B	11170
2378	GAAGAA G AACUCC	2569	20210	HBV-2378 Amb.Rz-6 stab2	g ₉ g ₉ a ₉ g ₉ uu gga L ucCCUUCaagga L ucCGGG uucuuc B	11171
2423	CGUCGCA G AAGAUCU	2570	20211	HBV-2423 Amb.Rz-7 stab2	a ₉ g ₉ a ₉ u ₉ g ₉ cuu gga L ucCCUUCaagga L ucCGGG ugcgacg B	11172
2426	GCAGAA G AUCUCA	2571	20212	HBV-2426 Amb.Rz-6 stab2	u ₉ g ₉ a ₉ g ₉ au gga L ucCCUUCaagga L ucCGGG uucugc B	11173
2426	CGCAGAA G AUCUCA	2572	20213	HBV-2426 Amb.Rz-7 stab2	u ₉ u ₉ g ₉ a ₉ g ₉ au gga L ucCCUUCaagga L ucCGGG uucugcg B	11174
2476	UAAGGU G GGAAC	2573	20214	HBV-2476 Amb.Rz-6 stab2	g ₉ u ₉ g ₉ u ₉ cc gga L ucCCUUCaagga L ucCGGG accuua B	11175
2477	UAAGGUG G GAAACUU	2574	20215	HBV-2477 Amb.Rz-7 stab2	a ₉ a ₉ g ₉ g ₉ uuc gga L ucCCUUCaagga L ucCGGG caccuua B	11176
2477	AAGGUG G GAAACU	2575	20216	HBV-2477 Amb.Rz-6 stab2	a ₉ g ₉ u ₉ u ₉ c gga L ucCCUUCaagga L ucCGGG caccuu B	11177
1607	UGCACGU C GCAUGGA	2576	20697	HBV-1607 Rz-7 allyl stab1 (7/4)	u ₉ c ₉ c ₉ a ₉ g ₉ ugc cUGAuaggccguuagccGaa Acgugca B	11178
1887	GUGCCU U GGGUGG	2577	20698	HBV-1887 Rz-6 allyl stab1 (6/4)	c ₉ c ₉ a ₉ c ₉ cc cUGAuaggccguuagccGaa Aggcac B	11179
1607	GCACGU C GCAUGG	2374	20699	HBV-1607 Rz-6 allyl stab1 (6/3)	c ₉ c ₉ a ₉ u ₉ gc cUGAuaggccguuagccGaa Acgugc B	11180
1607	UGCACGU C GCAUGGA	2576	20700	HBV-1607 Rz-7 allyl stab1 (7/3)	u ₉ c ₉ c ₉ a ₉ g ₉ ugc cUGAuaggccguuagccGaa Acgugca B	11181
1887	GUGCCU U GGGUGG	2577	20701	HBV-1887 Rz-6 allyl stab1 (6/3)	c ₉ c ₉ a ₉ c ₉ cc cUGAuaggccguuagccGaa Aggcac B	11182
1887	UGUGCCU U GGGUGGC	2420	20702	HBV-1887 Rz-7 allyl stab1 (7/3)	g ₉ c ₉ c ₉ a ₉ ccc cUGAuaggccguuagccGaa Aggcaca B	11183
313	CCAAAU U CGCAGUC	2346	22798	HBV-313 Rz-7 Ome stab1	gacugcg CUGAuAggcccguuagccGAA Anuuugg B	11184
408	UCUUCUU C UGCAUCC	2349	22799	HBV-408 Rz-7 Ome stab1	ggaugca CUGAuAggcccguuagccGAA Aggaaga B	11185
1756	AGGAGGU U AGGUUAA	2353	22800	HBV-1756 Rz-7 Ome stab1	uuuaccu CUGAuAggcccguuagccGAA Accuccu B	11186
10	CUCCACC A CUUUGCA	2356	22770	HBV-10 CHz-7 Ome stab1	uggaag CUGAuAggcccguuagccGAA Iguggag B	11187
335	UCCAGUC A CUCACCA	2357	22771	HBV-335 CHz-7 Ome stab1	uggugag CUGAuAggcccguuagccGAA Iacugga B	11188
273	CUUCUCU C AAUUUUC	2399	22645	HBV-273 Rz-7 allyl stab1 (7/3-GUUA)	g ₉ a ₉ a ₉ suu cUGAuaggccguuagccGaa Agagaag B	11189

273	CUUCUCU C AAUUUUC	2399	22646	HBV-273 Rz-7 allyl stab1 (7/4-GUUA)	G ₅ A ₅ A ₅ A ₅ uu cUGAuGagccgcuuaggccGaa Agagaag B	11190
273	CUUCUCU C AAUUUUC	2399	22648	HBV-273 Rz-7 allyl stab1 (7/3-GAAA)	G ₅ A ₅ A ₅ A ₅ uu cUGAuGagccgaaaggccGaa Agagaag B	11191
273	CUUCUCU C AAUUUUC	2578	22650	HBV-273 Rz-7 allyl stab1 (7/4-GAAA)	G ₅ A ₅ A ₅ A ₅ uu cUGAuGagccgaaaggccGaa Agagaag B	11192
273	UUCUCU C AAUUUU	2578	22644	HBV-273 Rz-6 allyl stab1 (6/3-GUUA)	a ₅ A ₅ A ₅ A ₅ uu cUGAuGagccgcuuaggccGaa Agagaa B	11193
273	UUCUCU C AAUUUU	2578	22647	HBV-273 Rz-6 allyl stab1 (6/3-GAAA)	a ₅ A ₅ A ₅ A ₅ uu cUGAuGagccgaaaggccGaa Agagaa B	11194
273	UUCUCU C AAUUUU	2579	22649	HBV-273 Rz-6 allyl stab1 (6/4-GAAA)	a ₅ A ₅ A ₅ A ₅ uu cUGAuGagccgaaaggccGaa Agagaa B	11195
350	ACCUUUU G UCCUCCA	2580	22714	HBV-350 GCL.Rz-7 5ribo stab3	uggagga uGAUg gcaUGcacuaugc gCG aacaggu B	11196
1253	CCUUUGU G UCUCUCU	2581	22715	HBV-1253 GCL.Rz-7 5ribo stab3	gaggaga uGAUg gcaUGcacuaugc gCG acaaagg B	11197
1856	UGUUAU G UCCUACU	2582	22716	HBV-1856 GCL.Rz-7 5ribo stab3	aguagga uGAUg gcaUGcacuaugc gCG augaaca B	11198
1966	GCCUUUCU G ACUUCUU	2583	22717	HBV-1966 GCL.Rz-7 5ribo stab3	aagaagu uGAUg gcaUGcacuaugc gCG agaaggc B	11199
3132	UCCUCCU G CCUCCAC	2584	22718	HBV-3132 GCL.Rz-7 5ribo stab3	guggagg uGAUg gcaUGcacuaugc gCG aggagga B	11200
332	AUCUCCA G UCACUCA	2579	22742	HBV-332 Zin.Rz-7 amino stab4	ugaguga gccgaaaggGagugagGuCu uggagau B	11201
350	ACCUUUU G UCCUCCA	2585	22743	HBV-350 Zin.Rz-7 amino stab4	uggagga gccgaaaggGagugagGuCu aacaggu B	11202
410	UUCUCU G CAUCCUG	2580	22744	HBV-410 Zin.Rz-7 amino stab4	caggaug gccgaaaggGagugagGuCu agaggaa B	11203
1253	CCUUUGU G UCUCUCU	2586	22745	HBV-1253 Zin.Rz-7 amino stab4	gaggaga gccgaaaggGagugagGuCu acaaagg B	11204
1754	GGAGGAG G UUAGGUU	2587	22746	HBV-1754 Zin.Rz-7 amino stab4	aaccuaa gccgaaaggGagugagGuCu cuccucc B	11205
407	AUCUCC U CUGCAUC	2588	22772	HBV-407 CHz-7 Ome stab1	gaugcag CUGAuGagccgcuuaggccGAA Igaagau B	11206
1848	UCAUCUC A UGUUAU	2589	22773	HBV-1848 CHz-7 Ome stab1	augaaca CUGAuGagccgcuuaggccGAA Iagauga B	11207
3124	GCAGCUC C UCCUCCU	2590	22774	HBV-3124 CHz-7 Ome stab1	aggagga CUGAuGagccgcuuaggccGAA Iagcugc B	11208
2165	GUCAGCU A UGUCAAC	2591	22801	HBV-2165 Rz-7 Ome stab1	guugaca CUGAuGagccgcuuaggccGAA Agcugac B	11209
2706	CCGUUU A UCCAGAG	2579	22802	HBV-2706 Rz-7 Ome stab1	cucugga CUGAuGagccgcuuaggccGAA Aauacgg B	11210
350	ACCUUUU G UCCUCCA	2584	22966	HBV-350 Dz-7 stab3	uggagga GGCTAGCTACAACGA aacaggu B	11211
332	AUCUCCA G UCACUCA	2592	22967	HBV-332 Dz-7 stab3	ugaguga GGCTAGCTACAACGA uggagau B	11212
1840	CUGCCUA A UCAUCUC	2593	22968	HBV-1840 Dz-7 stab3	gagauga GGCTAGCTACAACGA uaggcag B	11213
358	UCCUCCA A UUUGUCC	2580	22969	HBV-358 Dz-7 stab3	ggacaaa GGCTAGCTACAACGA uggagga B	11214
1253	CCUUUGU G UCUCUCU	2346	22970	HBV-1253 Dz-7 stab3	gaggaga GGCTAGCTACAACGA acaaagg B	11215
			20599	SAC	c ₅ A ₅ A ₅ u ₅ gu cUAGuGaccgaaaggGaa Aagagg B	10834

UPPER CASE = RIBO
UNDERLINE = DEOXY
lower case = 2'-O-methyl
I = inosine
s = phosphorothioate linkage
B = inverted deoxybasic residue
U = 2'-deoxy-2'-C-allyl Uridine
U = 2'-deoxy-2'-amino Uridine
C = 2'-deoxy-2'-amino Cytidine

Table XII: Group Designation and Dosage levels for HBV transgenic mouse study

Group	Compound	Dose	Number of Mice	Duration of Treatment
1	RPI.18341 (site 273)	100 mg/kg/day*	10F	14 days
2	RPI.18371 (site 1833)	100 mg/kg/day*	10F	14 days
3	RPI.18418 (site 1873)	100 mg/kg/day*	10F	14 days
4	RPI.18372 (site 1874)	100 mg/kg/day*	10F	14 days
5	Saline control	100 mg/kg/day*	10F	14 days
6	Untreated		10F	0 days

*administered via sc infusion using Alzet® mini-osmotic pumps

TABLE XIII: GROUP DESIGNATION AND DOSAGE LEVELS FOR HBV TRANSGENIC MOUSE STUDY

Group	Compound	Dose	Number of Mice	Duration of Treatment
1	RPI.18341 (site 273)	100 mg/kg/day*	15 (M or F)	14 days
2	RPI.18341 (site 273)	30 mg/kg/day*	15 (M or F)	14 days
3	RPI.18341 (site 273)	10 mg/kg/day*	15 (M or F)	14 days
4	RPI.18371 site 1833	100 mg/kg/day*	15 (M or F)	14 days
5	RPI.18371 site 1833	30 mg/kg/day*	15 (M or F)	14 days
6	RPI.18371 site 1833	10 mg/kg/day*	15 (M or F)	14 days
7	SAC (RPI.20599)	100 mg/kg/day*	15 (M or F)	14 days
8	SAC (RPI.20599)	30 mg/kg/day*	15 (M or F)	14 days
9	SAC (RPI.20599)	10 mg/kg/day*	15 (M or F)	14 days
10	Saline control	12 µl/day*	15 (M or F)	14 days
11	3TC® control	50 mg/kg/day, PO	15 (M or F)	14 days

*administered via sc infusion using Alzet® mini-osmotic pumps

Table XIV: HBV RT primer Decoy sequences

Length	Decoy Sequence	Seq ID No.
4	AUUC	11216
4	CAUU	11217
4	UCAU	11218
4	UUCA	11219
5	AUUCA	11220
5	CAUUC	11221
5	UCAUU	11222
5	UUCAU	11223
6	AUUCAU	11224
6	CAUUCA	11225
6	UCAUUC	11226
6	UUCAUU	11227
7	AUUCAUU	11228
7	CAUUCAU	11229
7	UCAUUCA	11230
7	UUCAUUC	11231
8	AUUCAUUC	11232
8	CAUUCAUU	11233
8	UCAUUCAU	11234
8	UUCAUUCA	11235
9	AUUCAUUCA	11236
9	CAUUCAUUC	11237
9	UCAUUCAUU	11238
9	UUCAUUCAU	11239
10	AUUCAUUCAU	11240
10	CAUUCAUUCA	11241
10	UCAUUCAUUC	11242
10	UUCAUUCAUU	11243
11	AUUCAUUCAUU	11244
11	CAUUCAUUCAU	11245
11	UCAUUCAUUCA	11246
11	UUCAUUCAUUC	11247
12	AUUCAUUCAUUC	11248
12	CAUUCAUUCAUU	11249
12	UCAUUCAUUCAU	11250
12	UUCAUUCAUUCA	11251
13	AUUCAUUCAUUCA	11252
13	CAUUCAUUCAUUC	11253
13	UCAUUCAUUCAUU	11254
13	UUCAUUCAUUCAU	11255
14	AUUCAUUCAUUCAU	11256
14	CAUUCAUUCAUUCA	11257
14	UCAUUCAUUCAUUC	11258
14	UUCAUUCAUUCAUU	11259
15	AUUCAUUCAUUCAUU	11260
15	CAUUCAUUCAUUCAU	11261

15	UCAUUCAUUCAUUC	11262
15	UUCAUUCAUUCAUUC	11263
16	AUUCAUUCAUUCAUUC	11264
16	CAUUCAUUCAUUCAUUC	11265
16	UCAUUCAUUCAUUCAU	11266
16	UUCAUUCAUUCAUUCA	11267
17	AUUCAUUCAUUCAUUCA	11268
17	CAUUCAUUCAUUCAUUC	11269
17	UCAUUCAUUCAUUCAUUC	11270
17	UUCAUUCAUUCAUUCAU	11271
18	AUUCAUUCAUUCAUUCAU	11272
18	CAUUCAUUCAUUCAUUCA	11273
18	UCAUUCAUUCAUUCAUUC	11274
18	UUCAUUCAUUCAUUCAUUC	11275
19	AUUCAUUCAUUCAUUCAUUC	11276
19	CAUUCAUUCAUUCAUUCAU	11277
19	UCAUUCAUUCAUUCAUUCA	11278
19	UUCAUUCAUUCAUUCAUUC	11279
20	AUUCAUUCAUUCAUUCAUUC	11280
20	CAUUCAUUCAUUCAUUCAUUC	11281
20	UCAUUCAUUCAUUCAUUCAU	11282
20	UUCAUUCAUUCAUUCAUUCA	11283
21	AUUCAUUCAUUCAUUCAUUCA	11284
21	CAUUCAUUCAUUCAUUCAUUC	11285
21	UCAUUCAUUCAUUCAUUCAUUC	11286
21	UUCAUUCAUUCAUUCAUUCAU	11287
22	CAUUCAUUCAUUCAUUCAUUCA	11288
22	UCAUUCAUUCAUUCAUUCAUUC	11289
22	UUCAUUCAUUCAUUCAUUCAUUC	11290
23	UCAUUCAUUCAUUCAUUCAUUCA	11291
23	UUCAUUCAUUCAUUCAUUCAUUC	11292
24	UUCAUUCAUUCAUUCAUUCAUUCA	11293

Table XV: Synthetic Nucleic acid molecules

RPI#	Alias	Sequence	SeqID
24961	HBV DR1 2'Oallyl P=S	g _s c _s a _s g _s a _s g _s g _s u _s g _s a _s a _s B	11294
24997	HBV DR1 2'Oallyl P=S control	a _s a _s g _s u _s g _s g _s a _s g _s a _s c _s g _s B	11295
24956	HBV 1866-1869 1x 2'Oallyl P=S	u _s u _s c _s a _s B	11296
24992	HBV 1866-1869 1x 2'Oallyl P=S control	a _s c _s u _s u _s B	11297
24941	HBV 1866-1869 2x 2'Oallyl P=S	u _s u _s c _s a _s u _s u _s c _s a _s B	11298
24959	HBV 1866-1869 2x 2'Oallyl P=S control	a _s c _s u _s u _s a _s c _s u _s u _s B	11299
24944	HBV 1866-1869 3x 2'Oallyl P=S	u _s u _s c _s a _s u _s u _s c _s a _s u _s u _s c _s a _s B	11300
24962	HBV 1866-1869 3x 2'Oallyl P=S control	a _s c _s u _s u _s a _s c _s u _s u _s a _s c _s u _s u _s B	11301
24945	HBV 1866-1869 4x 2'Oallyl P=S	u _s u _s c _s a _s u _s u _s c _s a _s u _s u _s c _s a _s u _s u _s c _s a _s B	11302
24963	HBV 1866-1869 4x 2'Oallyl P=S control	a _s c _s u _s u _s a _s c _s u _s u _s a _s c _s u _s u _s a _s c _s u _s u _s B	11303
24938	HBV 1866-1869 2'Oallyl P=S	u _s g _s a _s a _s B	11304
24974	HBV 1866-1869 2'Oallyl P=S control	a _s a _s g _s u _s B	11305
24940	HBV 1866-1872 2'Oallyl P=S	g _s c _s u _s u _s g _s a _s a _s B	11306
24958	HBV 1866-1872 2'Oallyl P=S control	a _s a _s g _s u _s u _s c _s g _s B	11307
24943	HBV 1866-1876 2'Oallyl P=S	g _s g _s a _s g _s g _s c _s u _s u _s g _s a _s a _s B	11308
24979	HBV 1866-1876 2'Oallyl P=S control	a _s a _s g _s u _s u _s c _s g _s g _s a _s g _s g _s B	11309
18341	HBV-273 UH.Rz-7 allyl stabl	g _s a _s a _s a _s auu cUGAuGaggccguuaggccGaa	10887
24588	HBV-273 UH.Rz-7 allyl stabl inact3 scraml (GUUA SAC)	a _s a _s u _s g _s agg cUAGuGacgccguuaggcgGaa	11310
24929	HBV 1866-1969 2'Omethyl	ugaaB	11311
24965	HBV 1866-1969 2'Omethyl control	aaguB	11312
24934	HBV 1866-1876 2'Omethyl	ggaggcuugaaB	11313
24970	HBV 1866-1876 2'Omethyl control	aaguucggaggB	11314
24976	HBV 1866-1872 2'Omethyl	gcuugaaB	11315
24949	HBV 1866-1872 2'Omethyl control	aaguucgB	11316
24952	HBV DR1 2'Omethyl	gcagaggugaaB	11317
24988	HBV DR1 2'Omethyl control	aaguggagacgB	11318
24947	HBV 1866-1869 1x 2'Omethyl	uucaB	11319
24983	HBV 1866-1869 1x 2'Omethyl control	acuuB	11320
24986	HBV 1866-1869 2x 2'Omethyl	uucuucaB	11321
24950	HBV 1866-1869 2x 2'Omethyl control	acuuacuuB	11322

24989	HBV 1866-1869 3x 2'Omethyl	uucauucauucaB	11323
24953	HBV 1866-1869 3x 2'Omethyl control	acuuacuuacuuB	11324
24936	HBV 1866-1869 4x 2'Omethyl	uucauucauucauucaB	11325
24954	HBV 1866-1869 4x 2'Omethyl control	acuuacuuacuuacuuB	11326
25639	HBV 5' EnI pos OMe P=S	B u _s u _s u _s c _s u _s a _s a _s g _s u _s a _s a _s a _s c _s a _s g _s u B	11327
25640	HBV 5' EnI neg OMe P=S	B a _s c _s u _s g _s u _s u _s u _s a _s c _s u _s u _s a _s g _s a _s a _s B	11328
25641	HBV 5' EnI sc OMe P=S	B a _s a _s g _s u _s a _s a _s c _s u _s c _s u _s a _s u _s g _s u _s a B	11329
25642	HBV 3' EnI pos OMe P=S	B u _s a _s c _s a _s u _s g _s a _s a _s c _s c _s u _s u _s u _s a _s c _s c _s c _s c _s B	11330
25643	HBV 3' EnI neg OMe P=S	B g _s g _s g _s u _s a _s a _s a _s g _s g _s u _s u _s c _s a _s u _s g _s u _s a B	11331
25644	HBV 3' EnI pos sc OMe P=S	B a _s c _s c _s u _s a _s u _s c _s g _s c _s c _s u _s a _s c _s u _s c _s u _s a _s a B	11332
25645	HBV 5' EnI neg sc OMe P=S	B u _s g _s a _s u _s a _s g _s c _s g _s g _s a _s u _s g _s a _s g _s a _s u _s u B	11333
25646	HBV DR1 pos OMe P=S	B u _s u _s c _s a _s c _s c _s u _s c _s u _s g _s c B	11334
25651	HBV 5' EnI pos Oallyl P=S	B u _s u _s u _s c _s u _s a _s a _s g _s u _s a _s a _s a _s c _s a _s g _s u B	11335
25652	HBV 5' EnI neg Oallyl P=S	B a _s c _s u _s g _s u _s u _s u _s a _s c _s u _s u _s a _s g _s a _s a _s B	11336
25653	HBV 5' EnI sc Oallyl P=S	B a _s a _s g _s u _s a _s a _s c _s u _s c _s u _s a _s u _s g _s u _s a B	11337
25654	HBV 3' EnI pos Oallyl P=S	B u _s a _s c _s a _s u _s g _s a _s a _s c _s c _s u _s u _s u _s a _s c _s c _s c _s c _s B	11338
25655	HBV 3' EnI neg Oallyl P=S	B g _s g _s g _s u _s a _s a _s a _s g _s g _s u _s u _s c _s a _s u _s g _s u _s a B	11339
25656	HBV 3' EnI pos sc Oallyl P=S	B a _s c _s c _s u _s a _s u _s c _s g _s c _s c _s u _s a _s c _s u _s c _s u _s a _s a B	11340
25657	HBV 5' EnI neg sc Oallyl P=S	B u _s g _s a _s u _s a _s g _s c _s g _s g _s a _s u _s g _s a _s g _s a _s u _s u B	11341
25658	HBV DR1 pos Oallyl P=S	B u _s u _s c _s a _s c _s c _s u _s c _s u _s g _s c B	11342

a, g, c, u = all 2'-O-allyl

a, g, c, u = 2'-O-methyl

U = 2'-C-allyl Uridine

S = phosphorothioate

B = inverted deoxybasic

Table XVI: Comparison of Tumor Weight to HBV DNA concentration in mice inoculated with HepG2.2.15 cells

Time point (days)	HBV DNA copies/mL serum	Tumor weight (milligrams)
1	Below detection	No tumor
1	Below detection	No tumor
1	Below detection	No tumor
1	Below detection	No tumor
7	Below detection	No tumor
7	Below detection	No tumor
7	Below detection	No tumor
7	Below detection	No tumor
14	Below detection	No tumor
14	Below detection	No tumor
14	Below detection	No tumor
14	Below detection	No tumor
35	356	33
35	125083	167
35	578	No tumor
35	386	56
42	493	No tumor
42	114431	790
42	94025	359
42	111882	647
49	189885	816
49	Below detection	No tumor
49	293	90
49	41477	2521

Table XVII: Comparison of Tumor Weight to HBV DNA concentration in mice inoculated with G418 resistant HepG2.2.15 cells

Time point (days)	HBV DNA copies/mL serum	Tumor weight (milligrams)
37	7000	1120.0
37	no sample	no sample
37	400000	1962.3
37	26000	558.5
37	380000	2286.0
37	100	317.2
37	52000	1429.0
37	100	427.4
37	26000	813.2
37	1400	631.6
37	186000	1101.5
37	134000	1573.0
37	17800	1040.0
37	16600	1327.2
37	8200	275.7
37	68000	632.8
37	24000	1090.0
37	58000	1082.7
37	12400	1116.3
37	100	763.3

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Table XVIII: HCV DNazyme and Substrate Sequence

Pos	Substrate	SEQ ID	DNAZYME	SEQ ID
10	UGGGGGCG A CACUCCAC	2594	GTGGAGTG GGCTAGCTACAACGA CGCCCCCA	11343
12	GGGGCGAC A CUCCACCA	2595	TGGTGGAG GGCTAGCTACAACGA GTCGCCCC	11344
17	GACACUCC A CCAUAGAU	2596	ATCTATGG GGCTAGCTACAACGA GGAGTGTC	11345
20	ACUCCACC A UAGAUAC	2597	GTGATCTA GGCTAGCTACAACGA GGTGGAGT	11346
24	CACCAUAG A UCACUCCC	2598	GGGAGTGA GGCTAGCTACAACGA CTATGGTG	11347
27	CAUAGAUC A CUCCCCUG	2599	CAGGGGAG GGCTAGCTACAACGA GATCTATG	11348
35	ACUCCCCU G UGAGGAAC	2600	GTTCTCTA GGCTAGCTACAACGA AGGGGAGT	11349
42	UGUGAGGA A CUACUGUC	2601	GACAGTAG GGCTAGCTACAACGA TCCTCACA	11350
45	GAGGAACU A CUGUCUUC	2602	GAAGACAG GGCTAGCTACAACGA AGTTCCTC	11351
48	GAACUACU G UCUUACAG	2603	CGTGAAGA GGCTAGCTACAACGA AGTAGTTC	11352
54	CUGUCUUC A CGCAGAAA	2604	TTTCTGCG GGCTAGCTACAACGA GAAGACAG	11353
56	GUCUACAC G CAGAAAGC	2605	GCTTTCTG GGCTAGCTACAACGA GTGAAGAC	11354
63	CGCAGAAA G CGUCUAGC	2606	GCTAGACG GGCTAGCTACAACGA TTTCTGCG	11355
65	CAGAAAGC G UCUAGCCA	2607	TGGCTAGA GGCTAGCTACAACGA GCTTTCTG	11356
70	AGCGUCUA G CCAUGGCG	2608	CGCCATGG GGCTAGCTACAACGA TAGACGCT	11357
73	GUCUAGCC A UGGCGUUA	2609	TAACGCCA GGCTAGCTACAACGA GGCTAGAC	11358
76	UAGCCAUG G CGUUAGUA	2610	TACTAACG GGCTAGCTACAACGA CATGGCTA	11359
78	GCCAUGGC G UUAGUAUG	2611	CATACTAA GGCTAGCTACAACGA GCCATGGC	11360
82	UGGCGUUA G UAUGAGUG	2612	CACTCATA GGCTAGCTACAACGA TAACGCCA	11361
84	GCGUUAGU A UGAGUGUC	2613	GACACTCA GGCTAGCTACAACGA ACTAACGC	11362
88	UAGUAUGA G UGUCUGUC	2614	GCACGACA GGCTAGCTACAACGA TCATACTA	11363
90	GUAUGAGU G UCGUGCAG	2615	CTGCACGA GGCTAGCTACAACGA ACTCATAC	11364
93	UGAGUGUC G UGCAGCCU	2616	AGGCTGCA GGCTAGCTACAACGA GACACTCA	11365
95	AGUGUCGU G CAGCCUCC	2617	GGAGGCTG GGCTAGCTACAACGA ACGACACT	11366
98	GUCGUGCA G CCUCCAGG	2618	CCTGGAGG GGCTAGCTACAACGA TGCACGAC	11367
107	CCUCCAGG A CCCCCCU	2619	AGGGGGGG GGCTAGCTACAACGA CCTGGAGG	11368
125	CCGGGAGA G CCAUAGUG	2620	CACTATGG GGCTAGCTACAACGA TCTCCCGG	11369
128	GGAGAGCC A UAGUGGUC	2621	GACCACTA GGCTAGCTACAACGA GGCTCTCC	11370
131	GAGCCAUA G UGGUCUGC	2622	GCAGACCA GGCTAGCTACAACGA TATGGCTC	11371
134	CCAUAGUG G UCUGCGGA	2623	TCCGCAGA GGCTAGCTACAACGA CACTATGG	11372
138	AGUGGUCU G CGGAACCG	2624	CGGTTCCG GGCTAGCTACAACGA AGACCACT	11373
143	UCUGCGGA A CCGGUGAG	2625	CTCACCGG GGCTAGCTACAACGA TCCGCAGA	11374
147	CGGAACCG G UGAGUACA	2626	TGTACTCA GGCTAGCTACAACGA CGGTTCCG	11375
151	ACCGGUGA G UACACCGG	2627	CCGGTGTA GGCTAGCTACAACGA TCACCGGT	11376
153	CGGUGAGU A CACCGGAA	2628	TTCCGGTG GGCTAGCTACAACGA ACTCACCG	11377
155	GUGAGUAC A CCGGAAUU	2629	AATTCCGG GGCTAGCTACAACGA GTACTCAC	11378
161	ACACCGGA A UUGCCAGG	2630	CCTGGCAA GGCTAGCTACAACGA TCCGGTGT	11379
164	CCGGAAUU G CCAGGACG	2631	CGTCCTGG GGCTAGCTACAACGA AATTCCGG	11380
170	UUGCCAGG A CGACCGGG	2632	CCC GGTCG GGCTAGCTACAACGA CCTGGCAA	11381
173	CCAGGACG A CCGGGUCC	2633	GGACCCGG GGCTAGCTACAACGA CGTCCTGG	11382
178	ACGACCGG G UCCUUUCU	2634	AGAAAGGA GGCTAGCTACAACGA CCGGTCGT	11383
190	UUUCUUGG A UCAACCCG	2635	CGGGTTGA GGCTAGCTACAACGA CCAAGAAA	11384
194	UUGGAUCA A CCCGCUCA	2636	TGAGCGGG GGCTAGCTACAACGA TGATCCAA	11385
198	AUCAACCC G CUCAAUGC	2637	GCATTGAG GGCTAGCTACAACGA GGGTTGAT	11386
203	CCCGCUCA A UGCCUGGA	2638	TCCAGGCA GGCTAGCTACAACGA TGAGCGGG	11387
205	CGCUCAAU G CCUGGAGA	2639	TCTCCAGG GGCTAGCTACAACGA ATTGAGCG	11388
213	GCCUGGAG A UUUGGGCG	2640	CGCCCAA GGCTAGCTACAACGA CTCCAGGC	11389
219	AGAUUUGG G CGUGCCCC	2641	GGGGCAGG GGCTAGCTACAACGA CCAAATCT	11390
221	AUUUGGGC G UGCCCCCG	2642	CGGGGGCA GGCTAGCTACAACGA GCCCAAAT	11391
223	UUGGGCGU G CCCCCGCG	2643	CGCGGGGG GGCTAGCTACAACGA ACGCCCAA	11392

229	GUGCCCC G CGAGACUG	2644	CAGTCTCG GGCTAGCTACAACGA GGGGGCAC	11393
234	CCCCGAG A CUGCUAGC	2645	GCTAGCAG GGCTAGCTACAACGA CTCGCGGG	11394
237	GCGAGACU G CUAGCCGA	2646	TCGGCTAG GGCTAGCTACAACGA AGTCTCGC	11395
241	GACUGCUA G CCGAGUAG	2647	CTACTCGG GGCTAGCTACAACGA TAGCAGTC	11396
246	CUAGCCGA G UAGUGUUG	2648	CAACACTA GGCTAGCTACAACGA TCGGCTAG	11397
249	GCCGAGUA G UGUUGGGU	2649	ACCCAACA GGCTAGCTACAACGA TACTCGGC	11398
251	CGAGUAGU G UUGGGUCG	2650	CGACCCAA GGCTAGCTACAACGA ACTACTCG	11399
256	AGUGUUGG G UCGCGAAA	2651	TTTCGCGA GGCTAGCTACAACGA CCAACACT	11400
259	GUUGGGUC G CGAAAGGC	2652	GCCTTTTCG GGCTAGCTACAACGA GACCCAAC	11401
266	GCGGAAA G CCUUGUGG	2653	CCACAAGG GGCTAGCTACAACGA CTTTCGCG	11402
271	AAGGCCUU G UGUACUG	2654	CAGTACCA GGCTAGCTACAACGA AAGGCCTT	11403
274	GCCUUGUG G UACUGCCU	2655	AGGCAGTA GGCTAGCTACAACGA CACAAGGC	11404
276	CUUGUGGU A CUGCCUGA	2656	TCAGGCAG GGCTAGCTACAACGA ACCACAAG	11405
279	GUGGUACU G CCUGAUAG	2657	CTATCAGG GGCTAGCTACAACGA AGTACCAC	11406
284	ACUGCCUG A UAGGGUGC	2658	GCACCCTA GGCTAGCTACAACGA CAGGCAGT	11407
289	CUGAUAGG G UGCUUGCG	2659	CGCAAGCA GGCTAGCTACAACGA CCTATCAG	11408
291	GAUAGGGU G CUUGCGAG	2660	CTCGCAAG GGCTAGCTACAACGA ACCCTATC	11409
295	GGUGUCUU G CGAGUGCC	2661	GGCACTCG GGCTAGCTACAACGA AAGCACCC	11410
299	GCUUGCGA G UGCCCGG	2662	CCGGGGCA GGCTAGCTACAACGA TCGCAAGC	11411
301	UUGCGAGU G CCCCAGGA	2663	TCCCGGGG GGCTAGCTACAACGA ACTCGCAA	11412
311	CCCGGGAG G UCUCGUAG	2664	CTACGAGA GGCTAGCTACAACGA CTCCCGGG	11413
316	GAGGUCUC G UAGACCGU	2665	ACGGTCTA GGCTAGCTACAACGA GAGACCTC	11414
320	UCUCGUAG A CCGUGCAC	2666	GTGCACGG GGCTAGCTACAACGA CTACGAGA	11415
323	CGUAGACC G UGCACCAU	2667	ATGGTGCA GGCTAGCTACAACGA GGTCTACG	11416
325	UAGACCGU G CACCAUGA	2668	TCATGGTG GGCTAGCTACAACGA ACGGTCTA	11417
327	GACCGUGC A CCAUGAGC	2669	GCTCATGG GGCTAGCTACAACGA GCACGGTC	11418
330	CGUGCACC A UGAGCAG	2670	CGTGCTCA GGCTAGCTACAACGA GGTGCACG	11419
334	CACCAUGA G CACGAAUC	2671	GATTCGTG GGCTAGCTACAACGA TCATGGTG	11420
336	CCAUGAGC A CGAAUCCU	2672	AGGATTCG GGCTAGCTACAACGA GCTCATGG	11421
340	GAGCACGA A UCCUAAAC	2673	GTTTAGGA GGCTAGCTACAACGA TCGTGCTC	11422
347	AAUCCUAA A CCUCAAG	2674	CTTTGAGG GGCTAGCTACAACGA TTAGGATT	11423
360	AAAGAAAA A CCAAACGU	2675	ACGTTTGG GGCTAGCTACAACGA TTTTCTTT	11424
365	AAAACCAA A CGUAACAC	2676	GTGTTACG GGCTAGCTACAACGA TTGGTTTT	11425
367	AACCAAAC G UAACACCA	2677	TGGTGTGA GGCTAGCTACAACGA GTTTGGTT	11426
370	CAACGUA A CACCAACC	2678	GGTTGGTG GGCTAGCTACAACGA TACGTTTG	11427
372	AACGUAAAC A CCAACCGC	2679	GCGGTTGG GGCTAGCTACAACGA GTTACGTT	11428
376	UAACACCA A CCGCCGCC	2680	GGCGGCGG GGCTAGCTACAACGA TGGTGTGA	11429
379	CACCAACC G CCGCCAC	2681	GTGGGCGG GGCTAGCTACAACGA GGTGGGTG	11430
382	CAACCGCC G CCCACAGG	2682	CCTGTGGG GGCTAGCTACAACGA GGCGGTTG	11431
386	CGCCGCC A CAGGACGU	2683	ACGTCTCG GGCTAGCTACAACGA GGGCGGCG	11432
391	CCCACAGG A CGUCAAGU	2684	ACTTGACG GGCTAGCTACAACGA CCTGTGGG	11433
393	CACAGGAC G UCAAGUUC	2685	GAAGTTGA GGCTAGCTACAACGA GTCCTGTG	11434
398	GACGUCAA G UUCCCGG	2686	CCCGGGAA GGCTAGCTACAACGA TTGACGTC	11435
406	GUUCCCGG G CGGUGGUC	2687	GACCAACG GGCTAGCTACAACGA CCGGGAAC	11436
409	CCCGGGCG G UGGUCAGA	2688	TCTGACCA GGCTAGCTACAACGA CGCCCGGG	11437
412	GGGCGGUG G UCAGAUUC	2689	CGATCTGA GGCTAGCTACAACGA CACCGCCC	11438
417	GUGGUCAG A UCGUUGGU	2690	ACCAACGA GGCTAGCTACAACGA CTGACCAC	11439
420	GUCAGAU G UUGGUGGA	2691	TCCACCAA GGCTAGCTACAACGA GATCTGAC	11440
424	GAUCGUUG G UGGAGUUU	2692	AAACTCCA GGCTAGCTACAACGA CAACGATC	11441
429	UUGGUGGA G UUUACCU	2693	CAGGTAAA GGCTAGCTACAACGA TCCACCAA	11442
433	UGGAGUUU A CCUGUUGC	2694	GCAACAGG GGCTAGCTACAACGA AAATCCA	11443
437	GUUUACCU G UGCCGCG	2695	CGCGGCAA GGCTAGCTACAACGA AGGTAAAC	11444
440	UACCGUU G CCGCGCAG	2696	CTGCGCGG GGCTAGCTACAACGA AACAGGTA	11445
443	CUGUUGCC G CGCAGGGG	2697	CCCCTGCG GGCTAGCTACAACGA GGCAACAG	11446
445	GUUGCCGC G CAGGGGCC	2698	GGCCCTG GGCTAGCTACAACGA GCGGCAAC	11447
451	GCGCAGGG G CCCCAGGU	2699	ACCTGGGG GGCTAGCTACAACGA CCCTGCGC	11448

458	GGCCCCAG G UUGGGUGU	2700	ACACCCAA GGCTAGCTACAACGA CTGGGGCC	11449
463	CAGGUUGG G UGUGCGCG	2701	CGCGCACA GGCTAGCTACAACGA CCAACCTG	11450
465	GGUUGGGU G UGCGCGCG	2702	CGCGCGCA GGCTAGCTACAACGA ACCCAACC	11451
467	UUGGGUGU G CGCGCGAC	2703	GTCGCGCG GGCTAGCTACAACGA ACACCCAA	11452
469	GGGUGUGC G CGCGACUA	2704	TAGTCGCG GGCTAGCTACAACGA GCACACCC	11453
471	GUGUGCGC G CGACUAGG	2705	CCTAGTCG GGCTAGCTACAACGA GCGCACAC	11454
474	UGCGCGCG A CUAGGAAG	2706	CTTCCTAG GGCTAGCTACAACGA CGCGCGCA	11455
483	CUAGGAAG A CUUCCGAG	2707	CTCGGAAG GGCTAGCTACAACGA CTTCCTAG	11456
491	ACUUCCGA G CGGUCGCA	2708	TGCGACCG GGCTAGCTACAACGA TCGGAAGT	11457
494	UCCGAGCG G UCGCAACC	2709	GGTTGCGA GGCTAGCTACAACGA CGCTCGGA	11458
497	GAGCGGUC G CAACCUCG	2710	CGAGGTTG GGCTAGCTACAACGA GACCGCTC	11459
500	CGGUCGCA A CCUCGUGG	2711	CCACGAGG GGCTAGCTACAACGA TCGGACCG	11460
505	GCAACCUC G UGGAAGGC	2712	GCCTTCCA GGCTAGCTACAACGA GAGGTTGC	11461
512	CGUGGAAG G CGACAACC	2713	GGTTGTCT GGCTAGCTACAACGA CTTCACG	11462
515	GGAAGGCG A CAACCUAU	2714	ATAGGTTG GGCTAGCTACAACGA CGCTTCC	11463
518	AGGCGACA A CCUAUCCC	2715	GGGATAGG GGCTAGCTACAACGA TGTCGCCT	11464
522	GACAACCU A UCCCAAG	2716	CTTGGGGA GGCTAGCTACAACGA AGGTTGTC	11465
531	UCCCAAG G CUCGCCGG	2717	CCGGCGAG GGCTAGCTACAACGA CTTGGGGA	11466
535	CAAGGCUC G CCGGCCCG	2718	CGGGCCGG GGCTAGCTACAACGA GAGCCTTG	11467
539	GCUCGCCG G CCGAGGG	2719	CCCTCGGG GGCTAGCTACAACGA CGGCGAGC	11468
547	GCCCGAGG G CAGGGCCU	2720	AGGCCCTG GGCTAGCTACAACGA CCTCGGGC	11469
552	AGGGCAGG G CCUGGGCU	2721	AGCCCAGG GGCTAGCTACAACGA CCTGCCCT	11470
558	GGGCCUGG G CUCAGCCC	2722	GGGCTGAG GGCTAGCTACAACGA CCAGGCCC	11471
563	UGGGUCUA G CCGGGGUA	2723	TACCCGGG GGCTAGCTACAACGA TGAGCCCA	11472
569	CAGCCCGG G UACCCUUG	2724	CAAGGGTA GGCTAGCTACAACGA CCGGGCTG	11473
571	GCCCGGGU A CCCUUGGC	2725	GCCAAGGG GGCTAGCTACAACGA ACCCGGGC	11474
578	UACCCUUG G CCCUCUA	2726	TAGAGGGG GGCTAGCTACAACGA CAAGGGTA	11475
586	GCCCCUCU A UGGCAAUG	2727	CATTGCCA GGCTAGCTACAACGA AGAGGGGC	11476
589	CCUCUAUG G CAAUGAGG	2728	CCTCATTG GGCTAGCTACAACGA CATAGAGG	11477
592	CUAUGGCA A UGAGGGCU	2729	AGCCCTCA GGCTAGCTACAACGA TGCCATAG	11478
598	CAAUGAGG G CUUAGGGU	2730	ACCCTAAG GGCTAGCTACAACGA CCTCATTG	11479
605	GGCUUAGG G UGGGCAGG	2731	CCTGCCCA GGCTAGCTACAACGA CCTAAGCC	11480
609	UAGGGUGG G CAGGAUGG	2732	CCATCCTG GGCTAGCTACAACGA CCACCCTA	11481
614	UGGGCAGG A UGGCUCCU	2733	AGGAGCCA GGCTAGCTACAACGA CCTGCCCA	11482
617	GCAGGAUG G CUCCUGUC	2734	GACAGGAG GGCTAGCTACAACGA CATCCTGC	11483
623	UGGCUCU G UCACCCCG	2735	CGGGGTGA GGCTAGCTACAACGA AGGAGCCA	11484
626	UCCUGUC A CCCC CGG	2736	CCGCGGGG GGCTAGCTACAACGA GACAGGAG	11485
631	GUCACCCC G CGGCUCCC	2737	GGGAGCCG GGCTAGCTACAACGA GGGGTGAC	11486
634	ACCCCGCG G CUCCCGGC	2738	GCCGGGAG GGCTAGCTACAACGA CGCGGGGT	11487
641	GGCUCCCG G CCUAGUUG	2739	CAACTAGG GGCTAGCTACAACGA CGGGAGCC	11488
646	CCGGCCUA G UUGGGGCC	2740	GGCCCCAA GGCTAGCTACAACGA TAGGCCGG	11489
652	UAGUUGGG G CCCACCG	2741	CCGTGGGG GGCTAGCTACAACGA CCCAACTA	11490
657	GGGGCCCC A CGGACCCC	2742	GGGGTCCG GGCTAGCTACAACGA GGGGCCCC	11491
661	CCCCACGG A CCCC GGC	2743	GCCGGGGG GGCTAGCTACAACGA CCGTGGGG	11492
668	GACCCCGG G CGUAGGUC	2744	GACCTACG GGCTAGCTACAACGA CGGGGGTC	11493
670	CCCCCGGC G UAGGUCGC	2745	GCGACCTA GGCTAGCTACAACGA GCCGGGGG	11494
674	CGGCGUAG G UGCGGUAA	2746	TTACGCGA GGCTAGCTACAACGA CTACGCCG	11495
677	CGUAGGUC G CGUAACUU	2747	AAGTTACG GGCTAGCTACAACGA GACCTACG	11496
679	UAGGUCGC G UAACUUGG	2748	CCAAGTTA GGCTAGCTACAACGA GCGACCTA	11497
682	GUCGCGUA A CUUGGGUA	2749	TACCCAAG GGCTAGCTACAACGA TACGCGAC	11498
688	UAACUUGG G UAAGGUCA	2750	TGACCTTA GGCTAGCTACAACGA CCAAGTTA	11499
693	UGGUUAAG G UCAUCGAU	2751	ATCGATGA GGCTAGCTACAACGA CTTACCCA	11500
696	GUAAGGUC A UCGAUACC	2752	GGTATCGA GGCTAGCTACAACGA GACCTTAC	11501
700	GGUCAUCG A UACCCUCA	2753	TGAGGGTA GGCTAGCTACAACGA CGATGACC	11502
702	UCAUCGAU A CCCUCACA	2754	TGTGAGGG GGCTAGCTACAACGA ATCGATGA	11503
708	AUACCCUC A CAUGCGGC	2755	GCCGCATG GGCTAGCTACAACGA GAGGGTAT	11504

710	ACCCUCAC A UGCGGCUU	2756	AAGCCGCA GGCTAGCTACAACGA GTGAGGGT	11505
712	CCUCACAU G CGGCUUCG	2757	CGAAGCCG GGCTAGCTACAACGA ATGTGAGG	11506
715	CACAUGCG G CUUCGCCG	2758	CGGCGAAG GGCTAGCTACAACGA CGCATGTG	11507
720	GCGGCUUC G CCGACCUC	2759	GAGGTCGG GGCTAGCTACAACGA GAAGCCGC	11508
724	CUUCGCCG A CCUCAUGG	2760	CCATGAGG GGCTAGCTACAACGA CGGCGAAG	11509
729	CCGACCUC A UGGGUUAC	2761	GTACCCCA GGCTAGCTACAACGA GAGGTCGG	11510
734	CUCAUGGG G UACAUUCC	2762	GGAATGTA GGCTAGCTACAACGA CCCATGAG	11511
736	CAUGGGGU A CAUCCCGC	2763	GCGGAATG GGCTAGCTACAACGA ACCCCATG	11512
738	UGGGGUAC A UUCCGCUC	2764	GAGCGGAA GGCTAGCTACAACGA GTACCCCA	11513
743	UACAUUCC G CUCGUCGG	2765	CCGACGAG GGCTAGCTACAACGA GGAATGTA	11514
747	UUCCGCUC G UCGGCGCC	2766	GGCGCCGA GGCTAGCTACAACGA GAGCGGAA	11515
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753	UCGUCGGC G CCCCCUUG	2768	CAAGGGGG GGCTAGCTACAACGA GCCGACGA	11517
766	CUUGGGAG G CACUGCCA	2769	TGGCAGTG GGCTAGCTACAACGA CTCCCAAG	11518
768	UGGGAGGC A CUGCCAGG	2770	CCTGGCAG GGCTAGCTACAACGA GCCTCCCA	11519
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785	GCCUGGC G AUGGCGU	2774	ACGCCATG GGCTAGCTACAACGA GCCAGGC	11523
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790	GGCGCAUG G CGUCCGGG	2776	CCCGGACG GGCTAGCTACAACGA CATGCGCC	11525
792	CGCAUGGC G UCCGGGUU	2777	AACCCGGA GGCTAGCTACAACGA GCCATGCG	11526
798	GCGUCCGG G UUCUGGAA	2778	TTCCAGAA GGCTAGCTACAACGA CCGGACGC	11527
808	UCUGGAAG A CGGCUGA	2779	TCACGCCG GGCTAGCTACAACGA CTTCAGAG	11528
811	GGAAGACG G CGUGAACU	2780	AGTTCACG GGCTAGCTACAACGA CGTCTTCC	11529
813	AAGACGGC G UGAACUUA	2781	ATAGTTCA GGCTAGCTACAACGA GCCGTCTT	11530
817	CGGCUGA A CUAUGCAA	2782	TTGCATAG GGCTAGCTACAACGA TCACGCCG	11531
820	CGUGAACU A UGCAACAG	2783	CTGTTGCA GGCTAGCTACAACGA AGTTACAG	11532
822	UGAACUUA G CAACAGGG	2784	CCCTGTTG GGCTAGCTACAACGA ATAGTTCA	11533
825	ACUAUGCA A CAGGGAU	2785	ATTCCCTG GGCTAGCTACAACGA TGCATAGT	11534
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888	GUCUGACC A UCCAGCC	2796	GGCTGGGA GGCTAGCTACAACGA GGTCAGAC	11545
894	CCAUCCCA G CCUCCGCU	2797	AGCGGAGG GGCTAGCTACAACGA TGGGATGG	11546
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911	UAUGAGGU G UGCAACGC	2801	GCGTTGCA GGCTAGCTACAACGA ACCTCATA	11550
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918	UGUGCAAC G CGUCCGGG	2804	CCCGGACG GGCTAGCTACAACGA GTTGACAC	11553
920	UGCAACGC G UCCGGGCU	2805	AGCCCGGA GGCTAGCTACAACGA GCCTTGCA	11554
926	GCGUCCGG G CUGUACCA	2806	TGGTACAG GGCTAGCTACAACGA CCGGACGC	11555
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931	CGGGCUGU G CCAUGUCA	2808	TGACATGG GGCTAGCTACAACGA ACAGCCCG	11557
934	GCUGUACC A UGUCACGA	2809	TCGTGACA GGCTAGCTACAACGA GGTACAGC	11558
936	UGUACCAU G UCACGAAC	2810	GTTCTGTA GGCTAGCTACAACGA ATGGTACA	11559
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949	GAACGAUU G CUCCAACU	2814	AGTTGGAG GGCTAGCTACAACGA AATCGTTC	11563
955	UUGCUCCA A CUCAAGCA	2815	TGCTTGAG GGCTAGCTACAACGA TGGAGCAA	11564
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990	ACAUGAUC A UGCACACC	2825	GGTGTGCA GGCTAGCTACAACGA GATCATGT	11574
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1004	ACCCCGGG G UGCGUGCC	2829	GGCACGCA GGCTAGCTACAACGA CCCGGGGT	11578
1006	CCCGGGGU G CGUGCCCU	2830	AGGGCAGC GGCTAGCTACAACGA ACCCGGGG	11579
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1454	AUUGUGAU G CUACUCUU	2944	AAGAGTAG GGCTAGCTACAACGA ATCACAAT	11693
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1488	ACACCUAC A CGACAGGG	2953	CCCTGTCT GGCTAGCTACAACGA GTAGGTGT	11702
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1597	GCACAUUA A CAGGACUG	2981	CAGTCCTG GGCTAGCTACAACGA TAATGTGC	11730
1602	UUAACAGG A CUGCCCUG	2982	CAGGGCAG GGCTAGCTACAACGA CCTGTTAA	11731
1605	ACAGGACU G CCCUGAAC	2983	GTTTCAGG GGCTAGCTACAACGA AGTCCTGT	11732
1612	UGCCCUGA A CUGCAAUG	2984	CATTGCAG GGCTAGCTACAACGA TCAGGGCA	11733
1615	CCUGAACU G CAAUGACU	2985	AGTCATTG GGCTAGCTACAACGA AGTTCAGG	11734
1618	GAACUGCA A UGACUCCC	2986	GGGAGTCA GGCTAGCTACAACGA TGCAGTTC	11735
1621	CUGCAAUG A CUCCCUCC	2987	GGAGGGAG GGCTAGCTACAACGA CATTGCAG	11736
1632	CCCUCCAA A CCGGUUUC	2988	GAACCCGG GGCTAGCTACAACGA TTGGAGGG	11737
1637	CAAACCGG G UUCAUUGC	2989	GCAATGAA GGCTAGCTACAACGA CCGTGTG	11738
1641	CCGGUUUC A UUGCUGCA	2990	TGCAGCAA GGCTAGCTACAACGA GAACCCGG	11739
1644	GGUUCAUU G CUGCACUG	2991	CAGTGCAG GGCTAGCTACAACGA AATGAACC	11740
1647	UCAUUGCU G CACUGUUC	2992	GAACAGTG GGCTAGCTACAACGA AGCAATGA	11741
1649	AUUGCUGC A CUGUUCUA	2993	TAGAACAG GGCTAGCTACAACGA GCAGCAAT	11742
1652	GCUGCACU G UUCUAUGC	2994	GCATAGAA GGCTAGCTACAACGA AGTGCAGC	11743
1657	ACUGUUCU A UGCACACA	2995	TGTGTGCA GGCTAGCTACAACGA AGAACAGT	11744
1659	UGUUCUAU G CACACAGG	2996	CCTGTGTG GGCTAGCTACAACGA ATAGAACA	11745
1661	UUCUAUGC A CACAGGUU	2997	AACCTGTG GGCTAGCTACAACGA GCATAGAA	11746
1663	CUAUGCAC A CAGGUUCA	2998	TGAACCTG GGCTAGCTACAACGA GTGCATAG	11747
1667	GCACACAG G UUCAACUC	2999	GAGTTGAA GGCTAGCTACAACGA CTGTGTGC	11748
1672	CAGGUUCA A CUCGUCCG	3000	CGGACGAG GGCTAGCTACAACGA TGAACCTG	11749
1676	UUCAACUC G UCCGGAUG	3001	CATCCGGA GGCTAGCTACAACGA GAGTTGAA	11750
1682	UCGUCCGG A UGCCACA	3002	TGTGGGCA GGCTAGCTACAACGA CCGACGCA	11751
1684	GUCCGGAU G CCCACAGC	3003	GCTGTGGG GGCTAGCTACAACGA ATCCGGAC	11752
1688	GGAUGCCC A CAGCGCUU	3004	AAGCGCTG GGCTAGCTACAACGA GGGCATCC	11753
1691	UGCCCACA G CGCUUGGC	3005	GCCAAGCG GGCTAGCTACAACGA TGTGGGCA	11754
1693	CCCACAGC G CUUGGCCA	3006	TGGCCAAG GGCTAGCTACAACGA GCTGTGGG	11755
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1705	GGCCAGCU G CCGCUCCA	3009	TGGAGCGG GGCTAGCTACAACGA AGCTGGCC	11758
1708	CAGCUGCC G CUCCAUG	3010	CAATGGAG GGCTAGCTACAACGA GGCAGCTG	11759
1713	GCCGCUCC A UUGACAAG	3011	CTTGTCAA GGCTAGCTACAACGA GGAGCGGC	11760
1717	CUCCAUG A CAAGUUCG	3012	CGAACTTG GGCTAGCTACAACGA CAATGGAG	11761
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1725	ACAAGUUC G CUCAGGGG	3014	CCCCTGAG GGCTAGCTACAACGA GATCTGT	11763
1733	GCUCAGGG G UGGGUCC	3015	GGACCCCA GGCTAGCTACAACGA CCCTGAGC	11764
1738	GGGGUGGG G UCCUAUCA	3016	TGATAGGA GGCTAGCTACAACGA CCCACCCC	11765
1743	GGGGUCCU A UCACCUAC	3017	GTAGGTGA GGCTAGCTACAACGA AGGACCCC	11766
1746	GUCCUAUC A CCUACACC	3018	GGTGTAGG GGCTAGCTACAACGA GATAGGAC	11767
1750	UAUCACCU A CACCGAGG	3019	CCTCGGTG GGCTAGCTACAACGA AGGTGATA	11768
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1759	CACCGAGG G CCACAACU	3021	AGTTGTGG GGCTAGCTACAACGA CCTCGGTG	11770
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1765	GGGCCACA A CUCGGACC	3023	GGTCCGAG GGCTAGCTACAACGA TGTGGCCC	11772
1771	CAACUCGG A CCAGAGGC	3024	GCCTCTGG GGCTAGCTACAACGA CCGAGTTG	11773
1778	GACCAGAG G CCCUAUUG	3025	CAATAGGG GGCTAGCTACAACGA CTCTGGTC	11774
1783	GAGGCCCU A UUGCUGGC	3026	GCCAGCAA GGCTAGCTACAACGA AGGGCCTC	11775
1786	GCCCUAUU G CUGGCACU	3027	AGTGCCAG GGCTAGCTACAACGA AATAGGGC	11776
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1937	ACGGACGU G CUGCUCU	3072	AGGAGCAG GGCTAGCTACAACGA ACGTCCGT	11821
1940	GACGUGCU G CUCCUCAA	3073	TTGAGGAG GGCTAGCTACAACGA AGCACGTC	11822
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1951	CCUCAACA A CACGCGGC	3075	GCCGCGTG GGCTAGCTACAACGA TGTGAGG	11824
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2214	UCUUUAAG G UUAGGAUG	3142	CATCCTAA GGCTAGCTACAACGA CTTAAAGA	11891
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2226	GGAUGUAU G UGGGGGGC	3146	GCCCCCCA GGCTAGCTACAACGA ATACATCC	11895
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2327	CCGCGUCU G UUGUCCAC	3170	GTGGACAA GGCTAGCTACAACGA AGCAGCGG	11919
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2354	CAAAUACU G CCCUGCUC	3178	GAGCAGGG GGCTAGCTACAACGA AGTATTTG	11927
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2397	CUGGUUUG A UCCAUCUC	3187	GAGATGGA GGCTAGCTACAACGA CAAACCAG	11936
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2431	CGUGCAAU A CCUGUACG	3197	CGTACAGG GGCTAGCTACAACGA ATTGCACG	11946
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2454	GGUCAGCG G UUGUCUCC	3204	GGAGACAA GGCTAGCTACAACGA CGCTGACC	11953
2457	CAGCGGUU G UCUCUUC	3205	GAAGGAGA GGCTAGCTACAACGA AACCGCTG	11954
2466	UCUCCUUC G CAAUCAA	3206	TTTGATTG GGCTAGCTACAACGA GAAGGAGA	11955
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2474	GCAAUCAA A UGGGAGUA	3208	TACTCCCA GGCTAGCTACAACGA TTGATTGC	11957
2480	AAAUGGGA G UAUGUCCU	3209	AGGACATA GGCTAGCTACAACGA TCCCATT	11958
2482	AUGGGAGU A UGUCCUGU	3210	ACAGGACA GGCTAGCTACAACGA ACTCCCAT	11959
2484	GGGAGUAU G UCCUGUUG	3211	CAACAGGA GGCTAGCTACAACGA ATACTCCC	11960
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2492	GUCCUGUU G CUUUUCCU	3213	AGGAAAAA GGCTAGCTACAACGA AACAGGAC	11962
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2514	UGGCAGAC G CGCGGUC	3216	GACGCGCG GGCTAGCTACAACGA GTCTGCCA	11965
2516	GCAGACGC G CGCGUCUG	3217	CAGACGCG GGCTAGCTACAACGA GCGTCTGC	11966
2518	AGACGCGC G CGUCUGUG	3218	CACAGACG GGCTAGCTACAACGA GCGCGTCT	11967
2520	ACGCGCGC G UCUGUGCC	3219	GGCACAGA GGCTAGCTACAACGA GCGCGCGT	11968
2524	GCGGUCU G UGCCUGUU	3220	AACAGGCA GGCTAGCTACAACGA AGACGCGC	11969
2526	GCGUCUGU G CCUGUUUG	3221	CAAACAGG GGCTAGCTACAACGA ACAGACGC	11970
2530	CUGUGCCU G UUUGUGGA	3222	TCCACAAA GGCTAGCTACAACGA AGGCACAG	11971
2534	GCGUGUUU G UGGAUGAU	3223	ATCATCCA GGCTAGCTACAACGA AAACAGGC	11972
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2541	UGUGGAUG A UGCUGUUG	3225	CAACAGCA GGCTAGCTACAACGA CATCCACA	11974
2543	UGGAUGAU G CUGUUGGU	3226	ACCAACAG GGCTAGCTACAACGA ATCATCCA	11975
2546	AUGAUGCU G UUGGUAGC	3227	GCTACCAA GGCTAGCTACAACGA AGCATCAT	11976
2550	UGCUGUUG G UAGCCCAG	3228	CTGGGCTA GGCTAGCTACAACGA CAACAGCA	11977
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2649	UCUUCUGU G CUGCCUGG	3249	CCAGGCAG GGCTAGCTACAACGA ACAGAAGA	11998
2652	UCUGUGCU G CCUGGUAC	3250	GTACCAGG GGCTAGCTACAACGA AGCACAGA	11999
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3339	CUGUCUCC G CCCGAAGG	3425	CCTTCGGG GGCTAGCTACAACGA GGAGACAG	12174
3357	GGAGGGAG A UACUCCUA	3426	TAGGAGTA GGCTAGCTACAACGA CTCCCTCC	12175
3359	AGGGAGAU A CUCCUAGG	3427	CCTAGGAG GGCTAGCTACAACGA ATCTCCCT	12176

3368	CUCCUAGG A CCAGCCGA	3428	TCGGCTGG GGCTAGCTACAACGA CCTAGGAG	12177
3372	UAGGACCA G CCGACAGU	3429	ACTGTCCG GGCTAGCTACAACGA TGGTCCTA	12178
3376	ACCAGCCG A CAGUCUUG	3430	CAAGACTG GGCTAGCTACAACGA CGGCTGGT	12179
3379	AGCCGACA G UCUUGAGG	3431	CCTCAAGA GGCTAGCTACAACGA TGTCGGCT	12180
3389	CUUGAGGG G CAGGGGUG	3432	CACCCCTG GGCTAGCTACAACGA CCCTCAAG	12181
3395	GGGCAGGG G UGGCGACU	3433	AGTCGCCA GGCTAGCTACAACGA CCCTGCCC	12182
3398	CAGGGGUG G CGACUCCU	3434	AGGAGTCG GGCTAGCTACAACGA CACCCTTG	12183
3401	GGGUGGCG A CUCCUCGC	3435	GCGAGGAG GGCTAGCTACAACGA CGCCACCC	12184
3408	GACUCCUC G CGCCCAUU	3436	AATGGGCG GGCTAGCTACAACGA GAGGAGTC	12185
3410	UCCUCGCG G CCCAUUAC	3437	GTAATGGG GGCTAGCTACAACGA GCGAGGAG	12186
3414	UCGCGCCC A UUACGGCC	3438	GGCCGTAA GGCTAGCTACAACGA GGGCGCGA	12187
3417	CGCCCAUU A CGGCCUAC	3439	GTAGGCCG GGCTAGCTACAACGA AATGGGCG	12188
3420	CCAUUACG G CCUACUCC	3440	GGAGTAGG GGCTAGCTACAACGA CGTAATGG	12189
3424	UACGGCCU A CUCCCAAC	3441	GTTGGGAG GGCTAGCTACAACGA AGGCCGTA	12190
3431	UACUCCCA A CAGACGCG	3442	CGCGTCTG GGCTAGCTACAACGA TGGGAGTA	12191
3435	CCCAACAG A CGCGGGGC	3443	GCCCCGCG GGCTAGCTACAACGA CTGTTGGG	12192
3437	CAACAGAC G CGGGCCU	3444	AGGCCCCG GGCTAGCTACAACGA GTCTGTTG	12193
3442	GACGCGGG G CCUGUUUG	3445	CAAACAGG GGCTAGCTACAACGA CCCGCGTC	12194
3446	CGGGGCCU G UUGGCUG	3446	CAGCCAAA GGCTAGCTACAACGA AGGCCCCG	12195
3451	CCUGUUUG G CUGCAUUA	3447	TAATGCAG GGCTAGCTACAACGA CAAACAGG	12196
3454	GUUUGGCU G CAUUAUCA	3448	TGATAATG GGCTAGCTACAACGA AGCCAAAC	12197
3456	UUGGCUGC A UUAUCACC	3449	GGTGATAA GGCTAGCTACAACGA GCAGCCAA	12198
3459	GCUGCAUU A UCACCAGC	3450	GCTGGETA GGCTAGCTACAACGA AATGCAGC	12199
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3522	UUUCCACC G CGACGCAG	3462	CTGCGTCG GGCTAGCTACAACGA GGTGAAA	12211
3525	CCACCGCG A CGCAGUCU	3463	AGACTCGG GGCTAGCTACAACGA CGCGTGG	12212
3527	ACCGCGAC G CAGUCUU	3464	AAAGACTG GGCTAGCTACAACGA GTCGCGGT	12213
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3547	AGCGACCU G CGUCAACG	3468	CGTTGACG GGCTAGCTACAACGA AGGTCGCT	12217
3549	CGACCUGC G UCAACGGC	3469	GCCGTTGA GGCTAGCTACAACGA GCAGGTCG	12218
3553	CUGCGUCA A CGGCUGU	3470	ACACGCCG GGCTAGCTACAACGA TGACGCAG	12219
3556	CGUCAACG G CGUGUCU	3471	AGCACACG GGCTAGCTACAACGA CGTTGACG	12220
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3562	CGGCGUGU G CUGGACUG	3474	CAGTCCAG GGCTAGCTACAACGA ACACGCCG	12223
3567	UGUGCUGG A CUGUCUAC	3475	GTAGACAG GGCTAGCTACAACGA CCAGCACA	12224
3570	GCUGGACU G UCUACCAC	3476	GTGGTAGA GGCTAGCTACAACGA AGTCCAGC	12225
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3695	UUGACACC A UGCACCUG	3506	CAGGTGCA GGCTAGCTACAACGA GGTGTCAA	12255
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3699	CACCAUGC A CCUGCGGC	3508	GCCGCAGG GGCTAGCTACAACGA GCATGGTG	12257
3703	AUGCACCU G CGGCGGCU	3509	AGCCGCCG GGCTAGCTACAACGA AGGTGCAT	12258
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3738	CGAGACAC G CUGAUGUC	3518	GACATCAG GGCTAGCTACAACGA GTGTCTCG	12267
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3772	GGGUGACA G CAGGGGA	3528	TCCCCCTG GGCTAGCTACAACGA TGTCACCC	12277
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3833	GGCGGUCC A CUGCUCUG	3538	CAGAGCAG GGCTAGCTACAACGA GGACCGCC	12287
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4243	CGGUGGUU G CUCUGGGG	3644	CCCCAGAG GGCTAGCTACAACGA AACCACCG	12393
4252	CUCUGGGG G CGCCUAUG	3645	CATAGGCG GGCTAGCTACAACGA CCCCAGAG	12394
4254	CUGGGGGG G CCUAUGAC	3646	GTCATAGG GGCTAGCTACAACGA CGCCCCAG	12395
4258	GGGCGCCU A UGACAUCA	3647	TGATGTGA GGCTAGCTACAACGA AGGCGCCC	12396
4261	CGCCUAUG A CAUCAUAA	3648	TTATGATG GGCTAGCTACAACGA CATAGGCG	12397
4263	CCUAUGAC A UCAUAAUG	3649	CATTATGA GGCTAGCTACAACGA GTCATAGG	12398
4266	AUGACAUC A UAAUGUGU	3650	ACACATTA GGCTAGCTACAACGA GATGTCAT	12399
4269	ACAUCAUA A UGUGUGAU	3651	ATCACACA GGCTAGCTACAACGA TATGATGT	12400

4271	AUCAAAU G UGUGAUGA	3652	TCATCACA GGCTAGCTACAACGA ATTATGAT	12401
4273	CAUAAUGU G UGAUGAGU	3653	ACTCATCA GGCTAGCTACAACGA ACATTATG	12402
4276	AAUGUGUG A UGAGUGCC	3654	GGCACTCA GGCTAGCTACAACGA CACACATT	12403
4280	UGUGAUGA G UGCCACUC	3655	GAGTGGCA GGCTAGCTACAACGA TCATCACA	12404
4282	UGAUGAGU G CCACUCAA	3656	TTGAGTGG GGCTAGCTACAACGA ACTCATCA	12405
4285	UGAGUGCC A CUCAAUUG	3657	CAATTGAG GGCTAGCTACAACGA GGCACCTA	12406
4290	GCCACUCA A UUGACUCG	3658	CGAGTCAA GGCTAGCTACAACGA TGAGTGGC	12407
4294	CUCAAUUG A CUCGACUU	3659	AAGTCGAG GGCTAGCTACAACGA CAATTGAG	12408
4299	UUGACUCG A CUUCCAUU	3660	AATGGAAG GGCTAGCTACAACGA CGAGTCAA	12409
4305	CGACUUC A UUUUGGGC	3661	GCCCAAAA GGCTAGCTACAACGA GGAAGTCG	12410
4312	CAUUUUGG G CAUCGGCA	3662	TGCCGATG GGCTAGCTACAACGA CCAAAATG	12411
4314	UUUUGGGG A UCGGCACA	3663	TGTGCCGA GGCTAGCTACAACGA GCCCAAAA	12412
4318	GGGCAUCG G CACAGUCC	3664	GGACTGTG GGCTAGCTACAACGA CGATGCCC	12413
4320	GCAUCGGC A CAGUCCUG	3665	CAGGACTG GGCTAGCTACAACGA GCCGATGC	12414
4323	UCGGCACA G UCCUGGAC	3666	GTCCAGGA GGCTAGCTACAACGA TGTGCCGA	12415
4330	AGUCCUGG A CCAAGCGG	3667	CCGCTTGG GGCTAGCTACAACGA CCAGGACT	12416
4335	UGGACCAA G CGGAGACG	3668	CGTCTCCG GGCTAGCTACAACGA TTGGTCCA	12417
4341	AAGCGGAG A CGGUGGA	3669	TCCAGCCG GGCTAGCTACAACGA CTCCGCTT	12418
4344	CGGAGACG G CUGGAGCG	3670	CGTCCAGG GGCTAGCTACAACGA CGTCTCCG	12419
4350	CGGUGGA G CGCGGCUC	3671	GAGCCGCG GGCTAGCTACAACGA TCCAGCCG	12420
4352	GCUGGAGC G CGGCUCGU	3672	ACGAGCCG GGCTAGCTACAACGA GCTCCAGC	12421
4355	GGAGCGCG G CUCGUCGU	3673	ACGACGAG GGCTAGCTACAACGA CGCGCTCC	12422
4359	CGCGGCUC G UCGUGCUC	3674	GAGCACGA GGCTAGCTACAACGA GAGCCGCG	12423
4362	GGCUCGUC G UGCUCGCC	3675	GGCAGCA GGCTAGCTACAACGA GACGAGCC	12424
4364	CUCGUCGU G CUCGCCAC	3676	GTGGCGAG GGCTAGCTACAACGA ACGACGAG	12425
4368	UCGUGCUC G CCACCGCU	3677	AGCGGTGG GGCTAGCTACAACGA GAGCACGA	12426
4371	UGCUCGCC A CCGCUACG	3678	CGTAGCGG GGCTAGCTACAACGA GGCGAGCA	12427
4374	UGGCCACC G CUACGCCU	3679	AGGCGTAG GGCTAGCTACAACGA GGTGGCGA	12428
4377	CCACCGCU A CGCCUCCG	3680	CGGAGGCG GGCTAGCTACAACGA AGCGGTGG	12429
4379	ACCGCUAC G CCUCCGGG	3681	CCCGGAGG GGCTAGCTACAACGA GTAGCGGT	12430
4388	CCUCCGGG A UCGGUCAC	3682	GTGACCGA GGCTAGCTACAACGA CCCGAGG	12431
4392	CGGGAUCG G UCACCGUG	3683	CACGGTGA GGCTAGCTACAACGA CGATCCCG	12432
4395	GAUCGGUC A CCGUGCCA	3684	TGGCACGG GGCTAGCTACAACGA GACCGATC	12433
4398	CGGUCACC G UGCCACAU	3685	ATGTGGCA GGCTAGCTACAACGA GGTGACCG	12434
4400	GUCACCGU G CCACAUCC	3686	GGATGTGG GGCTAGCTACAACGA ACGGTGAC	12435
4403	ACCGUGCC A CAUCCCAA	3687	TTGGGATG GGCTAGCTACAACGA GGCACGGT	12436
4405	CGUGCCAC A UCCCAACA	3688	TGTTGGGA GGCTAGCTACAACGA GTGGCACG	12437
4411	ACAUCCCA A CAUCGAGG	3689	CCTCGATG GGCTAGCTACAACGA TGGGATGT	12438
4413	AUCCCAAC A UCGAGGAG	3690	CTCCTCGA GGCTAGCTACAACGA GTTGGGAT	12439
4422	UCGAGGAG A UAGCCUUG	3691	CAAGGCTA GGCTAGCTACAACGA CTCCTCGA	12440
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4430	AUAGCCUU G UCCAACAC	3693	GTGTTGGA GGCTAGCTACAACGA AAGGCTAT	12442
4435	CUUGUCCA A CACGGAG	3694	CTCCGGTG GGCTAGCTACAACGA TGGACAAG	12443
4437	UGUCCAAC A CCGGAGAG	3695	CTCTCCGG GGCTAGCTACAACGA GTTGGACA	12444
4446	CCGGAGAG A UCCCCUUC	3696	GAAGGGGA GGCTAGCTACAACGA CTCTCCGG	12445
4456	CCCCUUCU A UGGCAAAG	3697	CTTTGCCA GGCTAGCTACAACGA AGAAGGGG	12446
4459	CUUCUAUG G CAAAGCCA	3698	TGGCTTTG GGCTAGCTACAACGA CATAGAAG	12447
4464	AUGGCAAA G CCAUCCCC	3699	GGGGATGG GGCTAGCTACAACGA TTTGCCAT	12448
4467	GCAAAGCC A UCCCCAUC	3700	GATGGGGA GGCTAGCTACAACGA GGCTTTGC	12449
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4479	CCAUCGAG A CCAUAAA	3702	TTTGATGG GGCTAGCTACAACGA CTCGATGG	12451
4482	UCGAGACC A UCAAAGGG	3703	CCCTTTGA GGCTAGCTACAACGA GGTCTCGA	12452
4496	GGGGGGAG G CAUCUCAU	3704	ATGAGATG GGCTAGCTACAACGA CTCCCCC	12453
4498	GGGGAGGC A UCUCAUCU	3705	AGATGAGA GGCTAGCTACAACGA GCCTCCCC	12454
4503	GGCAUCUC A UCUUCUGC	3706	GCAGAAGA GGCTAGCTACAACGA GAGATGCC	12455
4510	CAUCUUCU G CCAUUGCA	3707	TGGAATGG GGCTAGCTACAACGA AGAAGATG	12456

4513	CUUCUGCC A UUCCAAGA	3708	TCTTGGAA GGCTAGCTACAACGA GGCAGAAG	12457
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4528	GAAGAAAU G UGACGAGC	3710	GCTCGTCA GGCTAGCTACAACGA ATTTCTTC	12459
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4535	UGUGACGA G CUCGCUGC	3712	GCAGCGAG GGCTAGCTACAACGA TCGTCACA	12461
4539	ACGAGCUC G CUGCAAAG	3713	CTTTGCAG GGCTAGCTACAACGA GAGCTCGT	12462
4542	AGCUCGCU G CAAAGCUG	3714	CAGCTTTG GGCTAGCTACAACGA AGCGAGCT	12463
4547	GCUGCAAA G CUGUCGGG	3715	CCCGACAG GGCTAGCTACAACGA TTTGCAGC	12464
4550	GCAAAGCU G UCGGGCCU	3716	AGGCCCCG GGCTAGCTACAACGA AGCTTTGC	12465
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4562	GGCCUCGG A CUUAACGC	3718	GCGTTAAG GGCTAGCTACAACGA CCGAGGCC	12467
4567	CGGACUUA A CGCUGUAG	3719	CTACAGCG GGCTAGCTACAACGA TAAGTCCG	12468
4569	GACUUAAC G CUGUAGCG	3720	CGCTACAG GGCTAGCTACAACGA GTTAAGTC	12469
4572	UUAACGCU G UAGCGUUA	3721	ATACGCTA GGCTAGCTACAACGA AGCGTTAA	12470
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4579	UGUAGCGU A UUACCGGG	3724	CCCGGTAA GGCTAGCTACAACGA ACGCTACA	12473
4582	AGCGUAU A CCGGGGUC	3725	GACCCCGG GGCTAGCTACAACGA AATACGCT	12474
4588	UUACCGGG G UCUCGACG	3726	CGTCGAGA GGCTAGCTACAACGA CCGGTAA	12475
4594	GGGUCUCG A CGUGUCCG	3727	CGGACACG GGCTAGCTACAACGA CGAGACCC	12476
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4615	ACCGGCCA G CGGGGACG	3734	CGTCCCCG GGCTAGCTACAACGA TGGCCGGT	12483
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4623	GCGGGGAC G UCGUUGUC	3736	GACAACGA GGCTAGCTACAACGA GTCCCCGC	12485
4626	GGGACGUC G UUGUCGUG	3737	CACGACAA GGCTAGCTACAACGA GACGTCCC	12486
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4644	CAACAGAC G CUCUAUUG	3743	CATTAGAG GGCTAGCTACAACGA GTCTGTTG	12492
4650	ACGCUCUA A UGACGGGC	3744	GCCCCGTA GGCTAGCTACAACGA TAGAGCGT	12493
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4710	UCACCCAA A CAGUCGAC	3762	GTCGACTG GGCTAGCTACAACGA TTGGGTGA	12511
4713	CCCAAACA G UCGACUUC	3763	GAAGTCGA GGCTAGCTACAACGA TGTTGGG	12512

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4729	CAGCUUGG A CCGUACCU	3766	AGGTAGGG GGCTAGCTACAACGA CCAAGCTG	12515
4734	UGGACCCU A CCGUACCU	3767	GGTGAAGG GGCTAGCTACAACGA AGGGTCCA	12516
4740	CUACCUUC A CCAUUGAG	3768	CTCAATGG GGCTAGCTACAACGA GAAGGTAG	12517
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4760	ACGACCGU G CCCCAGA	3774	TCTTGGGG GGCTAGCTACAACGA ACGGTCGT	12523
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4770	CCCAAGAC G CAGUGUCC	3776	GGACACTG GGCTAGCTACAACGA GTCTGGG	12525
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4819	CAGGAGAG G CAUAUACA	3786	TGTATATG GGCTAGCTACAACGA CTCTCTTG	12535
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4829	AUAUACAG G UUUGUGAC	3790	GTCACAAA GGCTAGCTACAACGA CTGTATAT	12539
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4896	GCUAUGAC G CGGGAUGU	3806	ACATCCCG GGCTAGCTACAACGA GTCATAGC	12555
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4910	UGUGCUUG G UACGAGCU	3810	AGCTCGTA GGCTAGCTACAACGA CAAGCACA	12559
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5041	AGAUGCCC A CUUCUUGU	3840	ACAAGAAG GGCTAGCTACAACGA GGGCATCT	12589
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5055	UGUCCAG A CCAAGCAG	3842	CTGCTTGG GGCTAGCTACAACGA CTGGGACA	12591
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5091	ACCUGGUA G CAUACCAA	3848	TTGGTATG GGCTAGCTACAACGA TACCAGGT	12597
5093	CUGGUAGC A UACCAAGC	3849	GCTTGTA GGCTAGCTACAACGA GCTACCAG	12598
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5143	AUCGUGGG A UCAAAUGU	3862	ACATTTGA GGCTAGCTACAACGA CCCACGAT	12611
5148	GGGAUCAA A UGUGGAAG	3863	CTTCCACA GGCTAGCTACAACGA TTGATCCC	12612
5150	GAUCAAAU G UGGAAGUG	3864	CACTTCCA GGCTAGCTACAACGA ATTTGATC	12613
5156	AUGUGGAA G UGUCUCAC	3865	GTGAGACA GGCTAGCTACAACGA TTCCACAT	12614
5158	GUGGAAGU G UCUCACAC	3866	GTGTGAGA GGCTAGCTACAACGA ACTTCCAC	12615
5163	AGUGUCUC A CACGGCUA	3867	TAGCCGTG GGCTAGCTACAACGA GAGACACT	12616
5165	UGUCUCAC A CGGCUAAA	3868	TTTAGCCG GGCTAGCTACAACGA GTGAGACA	12617
5168	CUCACACG G CUAAAGCC	3869	GGCTTTAG GGCTAGCTACAACGA CGTGTGAG	12618
5174	CGGCUAAA G CCUACGCU	3870	AGCGTAGG GGCTAGCTACAACGA TTTAGCCG	12619
5178	UAAAGCCU A CGCUACAC	3871	GTGTAGCG GGCTAGCTACAACGA AGGCTTTA	12620
5180	AAGCCUAC G CUACACGG	3872	CCGTGTAG GGCTAGCTACAACGA GTAGGCTT	12621
5183	CCUACGCU A CACGGGCC	3873	GGCCCGTG GGCTAGCTACAACGA AGCGTAGG	12622
5185	UACGCUAC A CGGGCCAA	3874	TTGGCCCG GGCTAGCTACAACGA GTAGCGTA	12623
5189	CUACACGG G CCAACACC	3875	GGTGTGGG GGCTAGCTACAACGA CCGTGTAG	12624

5193	ACGGGCCA A CACCCUG	3876	CAGGGGTG GGCTAGCTACAACGA TGGCCCGT	12625
5195	GGGCCAAC A CCCUGCU	3877	AGCAGGGG GGCTAGCTACAACGA GTTGGCCC	12626
5201	ACACCCCU G CUGUAUAG	3878	CTATACAG GGCTAGCTACAACGA AGGGGTGT	12627
5204	CCCCUGCU G UAUAGGCU	3879	AGCCTATA GGCTAGCTACAACGA AGCAGGGG	12628
5206	CCUGCUGU A UAGGCUAG	3880	CTAGCCTA GGCTAGCTACAACGA ACAGCAGG	12629
5210	CUGUAUAG G CUAGGAGC	3881	GCTCCTAG GGCTAGCTACAACGA CTATACAG	12630
5217	GGCUAGGA G CCGUCCAA	3882	TTGGACGG GGCTAGCTACAACGA TCCTAGCC	12631
5220	UAGGAGCC G UCCAAAAU	3883	ATTTTGGG GGCTAGCTACAACGA GGCTCCTA	12632
5227	CGUCCAAA A UGAUGUCA	3884	TGACATCA GGCTAGCTACAACGA TTTGGACG	12633
5230	CCAAAUG A UGUCACCC	3885	GGGTGACA GGCTAGCTACAACGA CATTTTGG	12634
5232	AAAAUGAU G UCACCCUC	3886	GAGGGTGA GGCTAGCTACAACGA ATCATTTT	12635
5235	AUGAUGUC A CCCUCACA	3887	TGTGAGGG GGCTAGCTACAACGA GACATCAT	12636
5241	UCACCCUC A CACACCCC	3888	GGGGTGTG GGCTAGCTACAACGA GAGGGTGA	12637
5243	ACCCUCAC A CACCCCAU	3889	ATGGGGTG GGCTAGCTACAACGA GTGAGGGT	12638
5245	CCUCACAC A CCCCAUAA	3890	TTATGGGG GGCTAGCTACAACGA GTGTGAGG	12639
5250	CACACCCC A UAACCAAA	3891	TTTGGTTA GGCTAGCTACAACGA GGGGTGTG	12640
5253	ACCCCAUA A CCAAAUAC	3892	GTATTTGG GGCTAGCTACAACGA TATGGGGT	12641
5258	AUAACCAA A UACAUCAU	3893	ATGATGTA GGCTAGCTACAACGA TTGGTTAT	12642
5260	AACCAAAU A CAUCAUGA	3894	TCATGATG GGCTAGCTACAACGA ATTTGGTT	12643
5262	CCAAAUAC A UCAUGACA	3895	TGTCATGA GGCTAGCTACAACGA GTATTTGG	12644
5265	AAUACAUC A UGACAUGC	3896	GCATGTCA GGCTAGCTACAACGA GATGTATT	12645
5268	ACAUCAUG A CAUGCAUG	3897	CATGCATG GGCTAGCTACAACGA CATGATGT	12646
5270	AUCAUGAC A UGCAUGUC	3898	GACATGCA GGCTAGCTACAACGA GTCATGAT	12647
5272	CAUGACAU G CAUGUCGG	3899	CCGACATG GGCTAGCTACAACGA ATGTCATG	12648
5274	UGACAUGC A UGUCGGCU	3900	AGCCGACA GGCTAGCTACAACGA GCATGTCA	12649
5276	ACAUGCAU G UCGGCUA	3901	TCAGCCGA GGCTAGCTACAACGA ATGCATGT	12650
5280	GCAUGUCG G CUGACCCUG	3902	CAGGTCAG GGCTAGCTACAACGA CGCATGTC	12651
5284	GUCGGCUG A CCUGGAGG	3903	CCTCCAGG GGCTAGCTACAACGA CAGCCGAC	12652
5292	ACCUGGAG G UCGUCACC	3904	GGTGACGA GGCTAGCTACAACGA CTCCAGGT	12653
5295	UGGAGGUC G UCACCAGC	3905	GCTGGTGA GGCTAGCTACAACGA GACCTCCA	12654
5298	AGGUCGUC A CCAGCACC	3906	GGTGCTGG GGCTAGCTACAACGA GACGACCT	12655
5302	CGUCACCA G CACCUGGG	3907	CCCAGGTG GGCTAGCTACAACGA TGGTGACG	12656
5304	UCACCAGC A CCUGGGUG	3908	CACCCAGG GGCTAGCTACAACGA GCTGGTGA	12657
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5312	ACCUGGGU G CUAGUAGG	3910	CCTACTAG GGCTAGCTACAACGA ACCGAGGT	12659
5316	GGGUGCUA G UAGGUGGC	3911	GCCACCTA GGCTAGCTACAACGA TAGCACCC	12660
5320	GCUAGUAG G UGGCGUCC	3912	GGACGCCA GGCTAGCTACAACGA CTACTAGC	12661
5323	AGUAGGUG G CGUCCUGG	3913	CCAGGACG GGCTAGCTACAACGA CACCTACT	12662
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5334	UCCUGGCA G CUCUGACC	3916	GGTCAGAG GGCTAGCTACAACGA TGCCAGGA	12665
5340	CAGCUCUG A CCGCGUAU	3917	ATACGCGG GGCTAGCTACAACGA CAGAGCTG	12666
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5347	GACCGCGU A UUGCCUGA	3920	TCAGGCAA GGCTAGCTACAACGA ACGCGGTC	12669
5350	CGCGUAUU G CCUGACGA	3921	TCGTCAGG GGCTAGCTACAACGA AATACGCG	12670
5355	AUUGCCUG A CGACAGGC	3922	GCCTGTCT GGCTAGCTACAACGA CAGGCAAT	12671
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5370	GCAGCGUG G UCAUUGUG	3927	CACAATGA GGCTAGCTACAACGA CACGCTGC	12676
5373	GCGUGGUC A UUGUGGGC	3928	GCCCACAA GGCTAGCTACAACGA GACCACGC	12677
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5463	AGGAGUGU G CCUCACAC	3946	GTGTGAGG GGCTAGCTACAACGA AACTCCT	12695
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5534	CUCGGAUU G CUGCAAAC	3962	GTTTGCA G GGCTAGCTACAACGA AATCCGAG	12711
5537	GAUUGUCU G CAAACAGC	3963	GCTGTTTG GGCTAGCTACAACGA AGCAATCC	12712
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5595	AGUGGCGA G CCCUUGAG	3977	CTCAAGGG GGCTAGCTACAACGA TCGCCACT	12726
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5624	AAGCACAU G UGGAUUU	3983	AAATTCCA GGCTAGCTACAACGA ATGTGCTT	12732
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5659	CCUAGCAG G CUUGUCCA	3992	TGGACAAG GGCTAGCTACAACGA CTGCTAGG	12741
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5680	GCCUGGGA A CCCCAGCA	3996	TCGCGGGG GGCTAGCTACAACGA TCCCAGGC	12745
5685	GGAACCCC G CGAUAGCA	3997	TGCTATCG GGCTAGCTACAACGA GGGGTTCC	12746
5688	ACCCCGCG A UAGCAUCA	3998	TGATGCTA GGCTAGCTACAACGA CGCGGGGT	12747
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5693	GCGAUAGC A UCAUUGAU	4000	ATCAATGA GGCTAGCTACAACGA GCTATCGC	12749
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5705	UUGAUGGC A UUCACAGC	4004	GCTGTGAA GGCTAGCTACAACGA GCCATCAA	12753
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5712	CAUUCACA G CCUCCAUUC	4006	GATGGAGG GGCTAGCTACAACGA TGTGAATG	12755
5718	CAGCCUCC A UCACCAGC	4007	GCTGGTGA GGCTAGCTACAACGA GGAGGCTG	12756
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5725	CAUCACCA G CCCGCUCA	4009	TGAGCGGG GGCTAGCTACAACGA TGGTGATG	12758
5729	ACCAGCCC G CUCACCAC	4010	GTGGTGAG GGCTAGCTACAACGA GGGCTGGT	12759
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5870	GGGAAGGU G CUUGUAGA	4042	TCTACAAG GGCTAGCTACAACGA ACCTTCCC	12791
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5919	GUGCUCUC G UGGCCUUC	4054	GAAGGCCA GGCTAGCTACAACGA GAGAGCAC	12803
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5962	UACCGAGG A CCUGGUCA	4062	TGACCAGG GGCTAGCTACAACGA CCTCGGTA	12811
5967	AGGACCUG G UCAACUUA	4063	TAAGTTGA GGCTAGCTACAACGA CAGGTCTT	12812
5971	CCUGGUCA A CUUACUCC	4064	GGAGTAAG GGCTAGCTACAACGA TGACCAGG	12813
5975	GUCAACUU A CUCCUGC	4065	GCAGGGAG GGCTAGCTACAACGA AAGTTGAC	12814
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5985	UCCCUGCC A UCCUCUCU	4067	AGAGAGGA GGCTAGCTACAACGA GGCAGGGA	12816
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6063	GAGAGGGC G CUGUGCAG	4087	CTGCACAG GGCTAGCTACAACGA GCCCTCTC	12836
6066	AGGGCGCU G UGCAGUGG	4088	CCACTGCA GGCTAGCTACAACGA AGCGCCCT	12837
6068	GGCGCUGU G CAGUGGAU	4089	ATCCACTG GGCTAGCTACAACGA ACAGCGCC	12838
6071	GCUGUGCA G UGGAUGAA	4090	TTCATCCA GGCTAGCTACAACGA TGCACAGC	12839
6075	UGCAGUGG A UGAAUCGG	4091	CCGATTCA GGCTAGCTACAACGA CCACTGCA	12840
6079	GUGGAUGA A UCGGCUGA	4092	TCAGCCGA GGCTAGCTACAACGA TCATCCAC	12841
6083	AUGAAUCG G CUGAUAGC	4093	GCTATCAG GGCTAGCTACAACGA CGATTTCAT	12842
6087	AUCGGCUG A UAGCUUUC	4094	GAACGCTA GGCTAGCTACAACGA CAGCCGAT	12843
6090	GGCUGAUA G CGUUCGU	4095	AGCGAACG GGCTAGCTACAACGA TATCAGCC	12844
6092	CUGAUAGC G UUCGCUUC	4096	GAAGCGAA GGCTAGCTACAACGA GCTATCAG	12845
6096	UAGCGUUC G CUUCGCGG	4097	CCGCGAAG GGCTAGCTACAACGA GAACGCTA	12846
6101	UUCGCUUC G CGGGGCAA	4098	TTGCCCCG GGCTAGCTACAACGA GAAGCGAA	12847
6106	UUCGCGGG G CAACCAUG	4099	CATGGTTG GGCTAGCTACAACGA CCCGCGAA	12848

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6114	GCAACCAU G UCUCCCCC	4102	GGGGGAGA GGCTAGCTACAACGA ATGGTTGC	12851
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6125	UCCCCCAC G CACUAUGU	4104	ACATAGTG GGCTAGCTACAACGA GTGGGGGA	12853
6127	CCCCACGC A CUAUGUGC	4105	GCACATAG GGCTAGCTACAACGA GCGTGGGG	12854
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6132	CGCACUAU G UGCCUGAG	4107	CTCAGGCA GGCTAGCTACAACGA ATAGTGCG	12856
6134	CACUAUGU G CCUGAGAG	4108	CTCTCAGG GGCTAGCTACAACGA ACATAGTG	12857
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6145	UGAGAGCG A CGCAGCGG	4110	CCGCTGCG GGCTAGCTACAACGA CGCTCTCA	12859
6147	AGAGCGAC G CAGCGGCG	4111	CGCCGCTG GGCTAGCTACAACGA GTCGCTCT	12860
6150	GCGACGCA G CGGCGCGC	4112	GCGCGCCG GGCTAGCTACAACGA TGCGTCGC	12861
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6162	CGCGCUC A CACAAUUC	4117	GATTGTGT GGCTAGCTACAACGA GACGCGCG	12866
6164	CGCGUCAC A CAAAUCCU	4118	AGGATTTG GGCTAGCTACAACGA GTGACGCG	12867
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6206	CUGAGGAG G CUCCAUCA	4126	TGATGGAG GGCTAGCTACAACGA CTCCTCAG	12875
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6215	CUCCAUCA G UGGAUCAA	4128	TTGATCCA GGCTAGCTACAACGA TGATGGAG	12877
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6274	UGUUUGGG A CUGGAUUA	4142	ATATCCAG GGCTAGCTACAACGA CCCAAACA	12891
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6298	GUUGACUG A CUUCAAGA	4150	TCTTGAAG GGCTAGCTACAACGA CAGTCAAC	12899
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6311	AAGACCG G CUUCAGUC	4152	GACTGAAG GGCTAGCTACAACGA CAGGTCTT	12901
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6323	CAGUCCAA G CUCCUGCC	4154	GGCAGGAG GGCTAGCTACAACGA TTGGACTG	12903
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6338	CCGCGGUU G CCGGGAGU	4158	ACTCCCGG GGCTAGCTACAACGA AACCGCGG	12907
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6397	GGGAGACG G UAUCAUGC	4169	GCATGATA GGCTAGCTACAACGA CGTCTCCC	12918
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6419	ACCUGCCC A UGCGGAGC	4176	GCTCCGCA GGCTAGCTACAACGA GGGCAGGT	12925
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6953	CUGUCUGC G CCUUCUUC	4308	GAAGAAGG GGCTAGCTACAACGA GCAGACAG	13057
6966	CUUCGAAG G CGACAUAC	4309	GTATGTCT GGCTAGCTACAACGA CTTCGAAG	13058
6969	CGAAGGCG A CAUACAUU	4310	AATGTATG GGCTAGCTACAACGA CGCCTTCG	13059
6971	AAGGCGAC A UACAUUAC	4311	GTAATGTA GGCTAGCTACAACGA GTCGCCTT	13060
6973	GGCGACAU A CAUUAACC	4312	GGGTAATG GGCTAGCTACAACGA ATGTCGCC	13061
6975	CGACAUAC A UUACCCAA	4313	TTGGGTAA GGCTAGCTACAACGA GTATGTCT	13062
6978	CAUACAUU A CCCAAUUA	4314	ATATTGGG GGCTAGCTACAACGA AATGTATG	13063
6983	AUUACCCA A UAUGACUC	4315	GAGTCATA GGCTAGCTACAACGA TGGGTAAT	13064
6985	UACCCAAU A UGACUCCC	4316	GGGAGTCA GGCTAGCTACAACGA ATTGGGTA	13065
6988	CCAAUAUG A CUCCCCAG	4317	CTGGGGAG GGCTAGCTACAACGA CATATTGG	13066
6997	CUCCCCAG A CUUUGACC	4318	GGTCAAAG GGCTAGCTACAACGA CTGGGGAG	13067
7003	AGACUUUG A CCUCAUCG	4319	CGATGAGG GGCTAGCTACAACGA CAAAGTCT	13068
7008	UUGACCUC A UCGAGGCC	4320	GGCCTCGA GGCTAGCTACAACGA GAGGTCAA	13069
7014	UCAUCGAG G CCAACCUC	4321	GAGGTTGG GGCTAGCTACAACGA CTCGATGA	13070
7018	CGAGGCCA A CCUCCUGU	4322	ACAGGAGG GGCTAGCTACAACGA TGGCCTCG	13071
7025	AACCUCCU G UGGCGGCA	4323	TGCCGCCA GGCTAGCTACAACGA AGGAGGTT	13072

7028	CUCCUGUG G CGGCAGGA	4324	TCCTGCCG GGCTAGCTACAACGA CACAGGAG	13073
7031	CUGUGGCG G CAGGAGAU	4325	ATCTCCTG GGCTAGCTACAACGA CGCCACAG	13074
7038	GGCAGGAG A UGGCGGGU	4326	ACCGCCCA GGCTAGCTACAACGA CTCCTGCC	13075
7042	GGAGAUGG G CGGUAACA	4327	TGTTACCG GGCTAGCTACAACGA CCATCTCC	13076
7045	GAUGGGCG G UAACAUCA	4328	TGATGTTA GGCTAGCTACAACGA CGCCATC	13077
7048	GGGCGGUA A CAUCACUC	4329	GAGTGATG GGCTAGCTACAACGA TACCGCCC	13078
7050	GCGGUAAC A UCACUCGC	4330	GCGAGTGA GGCTAGCTACAACGA GTTACCGC	13079
7053	GUAACAUC A CUCGCGUG	4331	CACGCGAG GGCTAGCTACAACGA GATGTTAC	13080
7057	CAUCACUC G CGUGGAGU	4332	ACTCCAGG GGCTAGCTACAACGA GAGTGATG	13081
7059	UCACUCGC G UGGAGUCA	4333	TGATCCA GGCTAGCTACAACGA GCGAGTGA	13082
7064	CGCGUGGA G UCAGAGAA	4334	TTCTCTGA GGCTAGCTACAACGA TCCACGCG	13083
7072	GUCAGAGA A UAAGGUAG	4335	CTACCTTA GGCTAGCTACAACGA TCTCTGAC	13084
7077	AGAAUAAG G UAGUUACC	4336	GGTAACCT GGCTAGCTACAACGA CTTATTCT	13085
7080	AUAAGGUA G UUACCCUG	4337	CAGGGTAA GGCTAGCTACAACGA TACCTTAT	13086
7083	AGGUAGUU A CCUGGAC	4338	GTCCAGGG GGCTAGCTACAACGA AACTACCT	13087
7090	UACCCUGG A CUCUUUUG	4339	CAAAAGAG GGCTAGCTACAACGA CCAGGGTA	13088
7099	CUCUUUUG A CCCGCUUC	4340	GAAGCGGG GGCTAGCTACAACGA CAAAAGAG	13089
7103	UUUGACCC G CUUCGAGC	4341	GCTCGAAG GGCTAGCTACAACGA GGGTCAAA	13090
7110	CGCUUCGA G CGGAGGAG	4342	CTCCTCCG GGCTAGCTACAACGA TCGAAGCG	13091
7120	GGAGGAGG A UGAGAGAG	4343	CTCTCTCA GGCTAGCTACAACGA CCTCCTCC	13092
7131	AGAGAGAG G UGUCCAUI	4344	AATGGACA GGCTAGCTACAACGA CTCTCTCT	13093
7133	AGAGAGGU G UCCAUIUC	4345	GGAATGGA GGCTAGCTACAACGA ACCTCTCT	13094
7137	AGGUGUCC A UUCGCGCG	4346	CGCCGGAA GGCTAGCTACAACGA GGACACCT	13095
7143	CCAUUCCG G CGGAGAUC	4347	GATCTCCG GGCTAGCTACAACGA CGGAATGG	13096
7149	CGGCGGAG A UCCUGCGG	4348	CCGCAGGA GGCTAGCTACAACGA CTCCGCCG	13097
7154	GAGAUCCU G CGGAAAUC	4349	GATTTCCG GGCTAGCTACAACGA AGGATCTC	13098
7160	CUGCGGAA A UCCAAGAA	4350	TTCTTGGA GGCTAGCTACAACGA TTCCGCAG	13099
7169	UCCAAGAA G UUUCCUUC	4351	GAAGGAAA GGCTAGCTACAACGA TTCTTGGA	13100
7179	UUCCUUCA G CGUUACCC	4352	GGGTAACG GGCTAGCTACAACGA TGAAGGAA	13101
7181	CCUUCAGC G UUACCCAUI	4353	ATGGGTAA GGCTAGCTACAACGA GCTGAAGG	13102
7184	UCAGCGUU A CCAUAUUG	4354	CATATGGG GGCTAGCTACAACGA AACGCTGA	13103
7188	CGUUACCC A UAUGGGCA	4355	TGCCCCATA GGCTAGCTACAACGA GGGTAAACG	13104
7190	UUACCCAUI A UGGGCACG	4356	CGTGCCCA GGCTAGCTACAACGA ATGGGTAA	13105
7194	CCAUAUGG G CACGCCCG	4357	CGGGCGTG GGCTAGCTACAACGA CCATATGG	13106
7196	AUAUGGGC G CGCCGGA	4358	TCCGGGCG GGCTAGCTACAACGA GCCATAT	13107
7198	AUGGCGAC G CCCGAUUI	4359	AATCCGGG GGCTAGCTACAACGA GTGCCCAT	13108
7204	ACGCCCGG A UUACAACC	4360	GGTTGTAA GGCTAGCTACAACGA CCGGCGGT	13109
7207	CCCGGAUI A CAACCCUC	4361	GAGGGTTG GGCTAGCTACAACGA AATCCGGG	13110
7210	GAUUACA A CCCUCCAC	4362	GTGGAGGG GGCTAGCTACAACGA TGTAATCC	13111
7217	AACCCUCC A CUACUAGA	4363	TCTAGTAG GGCTAGCTACAACGA GGAGGGTT	13112
7220	CCUCCACU A CUAGAGCC	4364	GGCTCTAG GGCTAGCTACAACGA AGTGGAGG	13113
7226	CUACUAGA G CCCUGGAA	4365	TTCCAGGG GGCTAGCTACAACGA TCTAGTAG	13114
7237	CUGGAAAG A CCAGACU	4366	AGTCTGGG GGCTAGCTACAACGA CTTTCCAG	13115
7243	AGACCCAG A CUACGUCC	4367	GGACGTAG GGCTAGCTACAACGA CTGGGTCT	13116
7246	CCCAGACU A CGUCCCUUC	4368	GAGGGACG GGCTAGCTACAACGA AGTCTGGG	13117
7248	CAGACUAC G UCCCUCCG	4369	CGGAGGGA GGCTAGCTACAACGA GTAGTCTG	13118
7257	UCCCUCCG G UGUACAC	4370	GTGTACCA GGCTAGCTACAACGA CGGAGGGA	13119
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7264	GGUGGUAC A CGGGUGCC	4373	GGCACCCG GGCTAGCTACAACGA GTACCACC	13122
7268	GUACACGG G UGCCAUU	4374	AATGGGCA GGCTAGCTACAACGA CCGTGTAC	13123
7270	ACACGGGU G CCAUUGC	4375	GCAATGGG GGCTAGCTACAACGA ACCCGTGT	13124
7274	GGGUGCCC A UUGCCACC	4376	GGTGGAAC GGCTAGCTACAACGA GGGCACCC	13125
7277	UGCCCAUUI G CCACCUGC	4377	GCAGGTGG GGCTAGCTACAACGA AATGGGCA	13126
7280	CCAUUGCC A CCUGCCAA	4378	TTGGCAGG GGCTAGCTACAACGA GGCAATGG	13127
7284	UGCCACCU G CCAAGGCC	4379	GGCCTTGG GGCTAGCTACAACGA AGGTGGCA	13128

7290	CUGCCAAG G CCCCUCCA	4380	TGGAGGGG GGCTAGCTACAACGA CTTGGCAG	13129
7299	CCCUCCA A UACCACCU	4381	AGGTGGTA GGCTAGCTACAACGA TGGAGGGG	13130
7301	CCUCCA AU A CCACCUC	4382	GGAGGTGG GGCTAGCTACAACGA ATTGGAGG	13131
7304	CCAAUACC A CCUCCACG	4383	CGTGGAGG GGCTAGCTACAACGA GGTATTGG	13132
7310	CCACCUC A CGGAGGAA	4384	TTCCTCCG GGCTAGCTACAACGA GGAGGTGG	13133
7323	GGAAGAGG A CGGUUGUU	4385	AACAACCG GGCTAGCTACAACGA CCTCTTCC	13134
7326	AGAGGACG G UUGUUCUG	4386	CAGAACAA GGCTAGCTACAACGA CGTCCTCT	13135
7329	GGACGGUU G UUCUGACA	4387	TGTCAGAA GGCTAGCTACAACGA AACCGTCC	13136
7335	UUGUUCUG A CAGAGUCC	4388	GGACTCTG GGCTAGCTACAACGA CAGAACAA	13137
7340	CUGACAGA G UCCACCGU	4389	ACGGTGGA GGCTAGCTACAACGA TCTGTGAG	13138
7344	CAGAGUCC A CCGUGUCU	4390	AGACACGG GGCTAGCTACAACGA GGACTCTG	13139
7347	AGUCCACC G UGUCUUCU	4391	AGAAGACA GGCTAGCTACAACGA GGTGGACT	13140
7349	UCCACCGU G UCUUCUGC	4392	GCAGAAGA GGCTAGCTACAACGA ACGGTGGA	13141
7356	UGUCUUCU G CCUUGGCG	4393	CGCAAGG GGCTAGCTACAACGA AGAAGACA	13142
7362	CUGCCUUG G CGGAGCUC	4394	GAGCTCCG GGCTAGCTACAACGA CAAGGCAG	13143
7367	UUGGCGGA G CUCGCCAC	4395	GTGGCGAG GGCTAGCTACAACGA TCCGCCAA	13144
7371	CGGAGCUC G CCACAAAG	4396	CTTTGTGG GGCTAGCTACAACGA GAGCTCCG	13145
7374	AGCUCGCC A CAAAGACC	4397	GGTCTTTG GGCTAGCTACAACGA GCGTGGCT	13146
7380	CCACAAAG A CCUUCGGC	4398	GCCGAAGG GGCTAGCTACAACGA CTTTGTGG	13147
7387	GACCUUCG G CAGCUCUG	4399	CAGAGCTG GGCTAGCTACAACGA CGAAGGTC	13148
7390	CUUCGGCA G CUCUGAAU	4400	ATTGAGAG GGCTAGCTACAACGA TGCCGAAG	13149
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7400	UCUGAAUC A UCGGCCGC	4402	GCCGCCGA GGCTAGCTACAACGA GATTGAGA	13151
7404	AAUCAUCG G CCGCUGAU	4403	ATCAGCGG GGCTAGCTACAACGA CGATGATT	13152
7407	CAUCGGCC G CUGAUAGA	4404	TCTATCAG GGCTAGCTACAACGA GGCCGATG	13153
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7417	UGAUAGAG G UACGGCAA	4406	TTGCCGTA GGCTAGCTACAACGA CTCTATCA	13155
7419	AUAGAGGU A CGGCAACC	4407	GGTTGCCG GGCTAGCTACAACGA ACCTCTAT	13156
7422	GAGGUACG G CAACCGCC	4408	GGCGGTTG GGCTAGCTACAACGA CGTACCTC	13157
7425	GUACGGCA A CCGCCCCC	4409	GGGGGCGG GGCTAGCTACAACGA TGCCGTAC	13158
7428	CGGCAACC G CCCCCCCC	4410	GGGGGGGG GGCTAGCTACAACGA GGTTGCCG	13159
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7443	CCGACCAG A CCUCCA AU	4412	ATTGGAGG GGCTAGCTACAACGA CTGGTCGG	13161
7450	GACCUC A UGACGGUG	4413	CACCGTCA GGCTAGCTACAACGA TGGAGGTC	13162
7453	CUCCA AUG A CGGUGACG	4414	CGTACCGG GGCTAGCTACAACGA CATTGGAG	13163
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7466	GACGCAGG A UCCGACGU	4418	ACGTCGGA GGCTAGCTACAACGA CCTGCGTC	13167
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7473	GAUCCGAC G UUGAGUCG	4420	CGACTCAA GGCTAGCTACAACGA GTCGGATC	13169
7478	GACGUUGA G UCGUACUC	4421	GAGTACGA GGCTAGCTACAACGA TCAACGTC	13170
7481	GUUGAGUC G UACUCCUC	4422	GAGGAGTA GGCTAGCTACAACGA GACTCAAC	13171
7483	UGAGUCGU A CUCCUCUA	4423	TAGAGGAG GGCTAGCTACAACGA ACGACTCA	13172
7491	ACUCCUCU A UGCCCCCC	4424	GGGGGGCA GGCTAGCTACAACGA AGAGGAGT	13173
7493	UCCUCUAU G CCCCCCU	4425	AGGGGGGG GGCTAGCTACAACGA ATAGAGGA	13174
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7525	GGAUCCCG A UCUCAGCG	4428	CGCTGAGA GGCTAGCTACAACGA CGGGATCC	13177
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7548	CUUGGUCU A CCGUGAGC	4433	GCTCACGG GGCTAGCTACAACGA AGACCAAG	13182
7551	GGUCUACC G UGAGCGAA	4434	TTCGCTCA GGCTAGCTACAACGA GGTAGACC	13183
7555	UACCGUGA G CGAAGAGG	4435	CCTCTTCG GGCTAGCTACAACGA TCACGGTA	13184

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7578	AGGAUGUC G UCUGCUGC	4440	GCAGCAGA GGCTAGCTACAACGA GACATCCT	13189
7582	UGUCGUCU G CUGCUCGA	4441	TCGAGCAG GGCTAGCTACAACGA AGACGACA	13190
7585	CGUCUGCU G CUCGAUGU	4442	ACATCGAG GGCTAGCTACAACGA AGCAGACG	13191
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7659	CCAUCAAC G CGUUGAGC	4463	GCTCAACG GGCTAGCTACAACGA GTTGATGG	13212
7661	AUCAACGC G UUGAGCAA	4464	TTGCTCAA GGCTAGCTACAACGA GCGTTGAT	13213
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7679	UCUUUGCU G CGUCACCA	4468	TGGTGACG GGCTAGCTACAACGA AGCAAAGA	13217
7681	UUUGCUGC G UACCACA	4469	TGTGGTGA GGCTAGCTACAACGA GCAGCAA	13218
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7824	CAGUUAAG G CUAAACUU	4505	AAGTTTAG GGCTAGCTACAACGA CTTAACTG	13254
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7839	UUCUAUCC G UAGAGGAA	4508	TTCTCTTA GGCTAGCTACAACGA GGATAGAA	13257
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7852	GGAAGCCU G CAGACUGA	4510	TCAGTCTG GGCTAGCTACAACGA AGGCTTCC	13259
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7862	AGACUGAC G CCCCCACA	4513	TGTGGGGG GGCTAGCTACAACGA GTCAGTCT	13262
7868	ACGCCCCC A CAUUCGGC	4514	GCCGAATG GGCTAGCTACAACGA GGGGGCGT	13263
7870	GCCCCCAC A UUCGGCCA	4515	TGGCCGAA GGCTAGCTACAACGA GTGGGGGC	13264
7875	CACAUUCG G CCAGGUCC	4516	GGACCTGG GGCTAGCTACAACGA CGAATGTG	13265
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7894	AUUUGGUU A UGGGGCAA	4520	TTGCCCCA GGCTAGCTACAACGA AACCAAAT	13269
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7924	CCUAUCCA G CGGGGCCG	4526	CGGCCCGG GGCTAGCTACAACGA TGGATAGG	13275
7929	CCAGCGGG G CCGUCAAC	4527	GTTGACGG GGCTAGCTACAACGA CCCGCTGG	13276
7932	GCGGGGCC G UCAACCAC	4528	GTGGTTGA GGCTAGCTACAACGA GGCCCCGC	13277
7936	GGCCGUCA A CCACAUCC	4529	GGATGTGG GGCTAGCTACAACGA TGACGGCC	13278
7939	CGUCAACC A CAUCCGCU	4530	AGCGGATG GGCTAGCTACAACGA GGTTGACG	13279
7941	UCAACCAC A UCCGCUCC	4531	GGAGCGGA GGCTAGCTACAACGA GTGGTTGA	13280
7945	CCACAUCC G CUCCGUGU	4532	ACACGGAG GGCTAGCTACAACGA GGATGTGG	13281
7950	UCCGCUCC G UGUGGAAG	4533	CTTCCACA GGCTAGCTACAACGA GGAGCGGA	13282
7952	CGCUCCGU G UGGAAGGA	4534	TCCTTCCA GGCTAGCTACAACGA ACGGAGCG	13283
7960	GUGGAAGG A CUUGCUGG	4535	CCAGCAAG GGCTAGCTACAACGA CTTTCCAC	13284
7964	AAGGACUU G CUGGAAGA	4536	TCTTCCAG GGCTAGCTACAACGA AAGTCCTT	13285
7972	GCUGGAAG A CACUGAGA	4537	TCTCAGTG GGCTAGCTACAACGA CTTCCAGC	13286
7974	UGGAAGAC A CUGAGACA	4538	TGTCTCAG GGCTAGCTACAACGA GTCTTCCA	13287
7980	ACACUGAG A CACCAAUU	4539	AATTGGTG GGCTAGCTACAACGA CTCAGTGT	13288
7982	ACUGAGAC A CCAAUUGA	4540	TCAATTGG GGCTAGCTACAACGA GTCTCAGT	13289
7986	AGACACCA A UUGAUACC	4541	GGTATCAA GGCTAGCTACAACGA TGGTGTCT	13290
7990	ACCAAUUG A UACCACCA	4542	TGGTGGA GGCTAGCTACAACGA CAATTGGT	13291
7992	CAAUUGAU A CCACCAUC	4543	GATGGTGG GGCTAGCTACAACGA ATCAATTG	13292
7995	UUGAUACC A CCAUCAUG	4544	CATGATGG GGCTAGCTACAACGA GGTATCAA	13293
7998	AUACCACC A UCAUGGCA	4545	TGCCATGA GGCTAGCTACAACGA GGTGGTAT	13294
8001	CCACCAUC A UGGCAAAA	4546	TTTTGCCA GGCTAGCTACAACGA GATGGTGG	13295
8004	CCAUCAUG G CAAAAAUU	4547	ATTTTTTG GGCTAGCTACAACGA CATGATGG	13296

8011	GGCAAAAA A UGAGGUUU	4548	AAACCTCA GGCTAGCTACAACGA TTTTGTGCC	13297
8016	AAAUGAG G UUUUCUGC	4549	GCAGAAAA GGCTAGCTACAACGA CTCATTTT	13298
8023	GGUUUUCU G CGUCCAAC	4550	GTTGGACG GGCTAGCTACAACGA AGAAAACC	13299
8025	UUUUCUGC G UCCAACCA	4551	TGGTTGGA GGCTAGCTACAACGA GCAGAAAA	13300
8030	UGCGUCCA A CCAGAGAA	4552	TTCTCTGG GGCTAGCTACAACGA TGGACGCA	13301
8044	GAAAGGAG G CCGCAAGC	4553	GCTTGCGG GGCTAGCTACAACGA CTCCTTTC	13302
8047	AGGAGGCC G CAAGCCAG	4554	CTGGCTTG GGCTAGCTACAACGA GGCTCCT	13303
8051	GGCCGCAA G CCAGCUCG	4555	CGAGCTGG GGCTAGCTACAACGA TTGCGGCC	13304
8055	GCAAGCCA G CUCGCCUU	4556	AAGGCGAG GGCTAGCTACAACGA TGGCTTGC	13305
8059	GCCAGCUC G CCUUAUCG	4557	CGATAAGG GGCTAGCTACAACGA GAGTGGC	13306
8064	CUCGCCUU A UCGUGUUC	4558	GAACACGA GGCTAGCTACAACGA AAGGCGAG	13307
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8077	GUUCCCAG A CUUGGGGG	4561	CCCCCAAG GGCTAGCTACAACGA CTGGGAAC	13310
8085	ACUUGGGG G UUCGUGUG	4562	CACACGAA GGCTAGCTACAACGA CCCCAGT	13311
8089	GGGGGUUC G UGUGUGCG	4563	CGCACACA GGCTAGCTACAACGA GAACCCCC	13312
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8093	GUUCGUGU G UGCGAGAA	4565	TTCTCGCA GGCTAGCTACAACGA ACACGAAC	13314
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8106	AGAAAAUG G CCCUUUAC	4568	GTAAAGGG GGCTAGCTACAACGA CATTTTCT	13317
8113	GGCCCUUU A CGACGUGG	4569	CCACGTCG GGCTAGCTACAACGA AAAGGGCC	13318
8116	CCUUUACG A CGUGGUCU	4570	AGACCACG GGCTAGCTACAACGA CGTAAAGG	13319
8118	UUUACGAC G UGGUCUCC	4571	GGAGACCA GGCTAGCTACAACGA GTCGTAAA	13320
8121	ACGACGUG G UCUCACC	4572	GGTGGAGA GGCTAGCTACAACGA CACGTCGT	13321
8127	UGGUCUCC A CCCUCCU	4573	AGGAAGGG GGCTAGCTACAACGA GGAGACCA	13322
8139	UUCUCAG G CCGUGAUG	4574	CATCACGG GGCTAGCTACAACGA CTGAGGAA	13323
8142	CUCAGGCC G UGAUGGGC	4575	GCCCATCA GGCTAGCTACAACGA GGCTGAG	13324
8145	AGGCCGUG A UGGGCUCU	4576	AGAGCCCA GGCTAGCTACAACGA CACGGCCT	13325
8149	CGUGAUGG G CUCUUCAU	4577	ATGAAGAG GGCTAGCTACAACGA CCATCACG	13326
8156	GGCUCUUC A UACGGAUU	4578	AATCCGTA GGCTAGCTACAACGA GAAGAGCC	13327
8158	CUCUUCAU A CGGAUUC	4579	GGAATCCG GGCTAGCTACAACGA ATGAAGAG	13328
8162	UCAUACGG A UCCAGUA	4580	TACTGGAA GGCTAGCTACAACGA CCGTATGA	13329
8168	GGAUUCCA G UACUCUCC	4581	GGAGAGTA GGCTAGCTACAACGA TGGAAATC	13330
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8183	CCUGGGCA G CGGGUUGA	4584	TCAACCCG GGCTAGCTACAACGA TGCCAGG	13333
8187	GGCAGCGG G UUGAGUUC	4585	GAAGTCAA GGCTAGCTACAACGA CCGTGCC	13334
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8224	AAAGAAAU G CCCUAUGG	4592	CCATAGGG GGCTAGCTACAACGA ATTCTTT	13341
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8233	CCCUAUGG G CUUUGCAU	4594	ATGCAAAG GGCTAGCTACAACGA CCATAGGG	13343
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8240	GGCUUUGC A UAUGACAC	4596	GTGTCATA GGCTAGCTACAACGA GCAAAGCC	13345
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8245	UGCAUAUG A CACCCGCU	4598	AGCGGGTG GGCTAGCTACAACGA CATATGCA	13347
8247	CAUAUGAC A CCCGUGU	4599	ACAGCGGG GGCTAGCTACAACGA GTCATATG	13348
8251	UGACACCC G CUGUUCG	4600	CGAAACAG GGCTAGCTACAACGA GGGTGTCA	13349
8254	CACCCGCU G UUUCGACU	4601	AGTCGAAA GGCTAGCTACAACGA AGCGGGTG	13350
8260	CUGUUCG A CUCAACAG	4602	CTGTTGAG GGCTAGCTACAACGA CGAAACAG	13351
8265	UCGACUCA A CAGUCACC	4603	GGTGACTG GGCTAGCTACAACGA TGAGTCGA	13352

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8278	CACCGAGA G UGACAUCC	4606	GGATGTCA GGCTAGCTACAACGA TCTCGGTG	13355
8281	CGAGAGUG A CAUCCGUG	4607	CACGGATG GGCTAGCTACAACGA CACTCTCG	13356
8283	AGAGUGAC A UCCGUGUC	4608	GACACGGA GGCTAGCTACAACGA GTCACTCT	13357
8287	UGACAUCC G UGUCGAGG	4609	CCTCGACA GGCTAGCTACAACGA GGATGTCA	13358
8289	ACAUCCGU G UCGAGGAG	4610	CTCCTCGA GGCTAGCTACAACGA ACGGATGT	13359
8297	GUCGAGGA G UCAAUUUA	4611	TAAATTGA GGCTAGCTACAACGA TCCTCGAC	13360
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8309	AUUUACCA A UGUUGUGA	4614	TCACAACA GGCTAGCTACAACGA TGGTAAAT	13363
8311	UUACCAAU G UUGUGACU	4615	AGTCACAA GGCTAGCTACAACGA ATTGGTAA	13364
8314	CCAAUGUU G UGACUUGG	4616	CCAAGTCA GGCTAGCTACAACGA AACATTGG	13365
8317	AUGUUGUG A CUUGGCC	4617	GGGCCAAG GGCTAGCTACAACGA CACAACAT	13366
8322	GUGACUUG G CCCCCGAA	4618	TTCGGGGG GGCTAGCTACAACGA CAAGTCAC	13367
8331	CCCCCGAA G CCAGACAG	4619	CTGTCTGG GGCTAGCTACAACGA TTCGGGGG	13368
8336	GAAGCCAG A CAGGCCAU	4620	ATGGCCTG GGCTAGCTACAACGA CTGGCTTC	13369
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8343	GACAGGCC A UAAGGUCG	4622	CGACCTTA GGCTAGCTACAACGA GGCCTGTC	13371
8348	GCCAUAAG G UCGCUCAC	4623	GTGAGCGA GGCTAGCTACAACGA CTTATGGC	13372
8351	AUAAGGUC G CUCACAGA	4624	TCTGTGAG GGCTAGCTACAACGA GACCTTAT	13373
8355	GGUCGCUC A CAGAGCGG	4625	CCGCTCTG GGCTAGCTACAACGA GAGCGACC	13374
8360	CUCACAGA G CGGCUUUA	4626	TAAAGCCG GGCTAGCTACAACGA TCTGTGAG	13375
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8368	GCGGCUUU A UAUCGGGG	4628	CCCCGATA GGCTAGCTACAACGA AAAGCCCG	13377
8370	GGCUUUAU A UCGGGGGU	4629	ACCCCGGA GGCTAGCTACAACGA ATAAAGCC	13378
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8413	CUGCGGUU A UCGCCGGU	4637	ACCGCGGA GGCTAGCTACAACGA AACCGCAG	13386
8416	CGGUUAUC G CCGGUGCC	4638	GGCACCGG GGCTAGCTACAACGA GATAACCG	13387
8420	UAUCGCCG G UGCCGCGC	4639	GCGCGGCA GGCTAGCTACAACGA CGGCGATA	13388
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8425	CCGGUGCC G CGCGAGCG	4641	CGCTCGCG GGCTAGCTACAACGA GGCACCGG	13390
8427	GGUGCCCG G CGAGCGGC	4642	GCCGCTCG GGCTAGCTACAACGA GCGGCACC	13391
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8434	CGCGAGCG G CGUGCUGA	4644	TCAGCACG GGCTAGCTACAACGA CGCTCGCG	13393
8436	CGAGCGGC G UGCUGACG	4645	CGTCAGCA GGCTAGCTACAACGA GCCGCTCG	13394
8438	AGCGGCGU G CUGACGAC	4646	GTCTGTAG GGCTAGCTACAACGA ACGCCGCT	13395
8442	GCGUGCUG A CGACCAGC	4647	GCTGGTCG GGCTAGCTACAACGA CAGCACGC	13396
8445	UGCUGACG A CCAGCUGU	4648	ACAGCTGG GGCTAGCTACAACGA CGTCAGCA	13397
8449	GACGACCA G CUGUGGUA	4649	TACCACAG GGCTAGCTACAACGA TGGTCGTC	13398
8452	GACCAGCU G UGUAAUA	4650	TATTACCA GGCTAGCTACAACGA AGCTGGTC	13399
8455	CAGCUGUG G UAAUACCC	4651	GGGTATTA GGCTAGCTACAACGA CACAGCTG	13400
8458	CUGUGGUA A UACCCUCA	4652	TGAGGGTA GGCTAGCTACAACGA TACCACAG	13401
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8466	AUACCCUC A CAUGUUAU	4654	GTAACATG GGCTAGCTACAACGA GAGGGTAT	13403
8468	ACCCUCAC A UGUUAUUU	4655	AAGTAACA GGCTAGCTACAACGA GTGAGGTT	13404
8470	CCUCACAU G UUACUUGA	4656	TCAAGTAA GGCTAGCTACAACGA ATGTGAGG	13405
8473	CACAUUUU A CUUGAAAG	4657	CTTTCAAG GGCTAGCTACAACGA AACATGTG	13406
8481	ACUUGAAA G CCUCUGCG	4658	CGCAGAGG GGCTAGCTACAACGA TTTCAAGT	13407
8487	AAGCCUCU G CGGCCUGU	4659	ACAGGCCG GGCTAGCTACAACGA AGAGGCTT	13408

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8499	CCUGUCGA G CUGCGAAG	4662	CTTCGCAG GGCTAGCTACAACGA TCGACAGG	13411
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8515	GUCCAGG A CUGCACGA	4665	TCGTGCAG GGCTAGCTACAACGA CCTGGAGC	13414
8518	CCAGGACU G CACGAUGC	4666	GCATCGTG GGCTAGCTACAACGA AGTCCTGG	13415
8520	AGGACUGC A CGAUGCUC	4667	GAGCATCG GGCTAGCTACAACGA GCAGTCCT	13416
8523	ACUGCACG A UGCUCGUG	4668	CACGAGCA GGCTAGCTACAACGA CGTGCAGT	13417
8525	UGCACGAU G CUCGUGUG	4669	CACACGAG GGCTAGCTACAACGA ATCGTGCA	13418
8529	CGAUGCUC G UGUGUGGA	4670	TCCACACA GGCTAGCTACAACGA GAGCATCG	13419
8531	AUGCUCGU G UGUGGAGA	4671	TCTCCACA GGCTAGCTACAACGA ACGAGCAT	13420
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8539	GUGUGGAG A CGACCUGG	4673	CCAGGTCG GGCTAGCTACAACGA CTCCACAC	13422
8542	UGGAGACG A CCUGGUCG	4674	CGACCAGG GGCTAGCTACAACGA CGTCTCCA	13423
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8550	ACCUGGUC G UUAUCUGU	4676	ACAGATAA GGCTAGCTACAACGA GACCAGGT	13425
8553	UGGUCGUU A UGUGGAA	4677	TTCACAGA GGCTAGCTACAACGA AACGACCA	13426
8557	CGUUAUCU G UGAAAGUG	4678	CACTTTCA GGCTAGCTACAACGA AGATAACG	13427
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8565	GUGAAAGU G CGGGGACC	4680	GGTCCCCG GGCTAGCTACAACGA ACTTTTAC	13429
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8581	CCAAGAGG A CGCGGCGA	4682	TCGCGCGG GGCTAGCTACAACGA CCTCTTGG	13431
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8598	GCCUACGA G UCUUACG	4687	CGTGAAGA GGCTAGCTACAACGA TCGTAGGC	13436
8604	GAGUCUUC A CGGAGGCU	4688	AGCCTCCG GGCTAGCTACAACGA GAAGACTC	13437
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8613	CGGAGGCU A UGACUAGG	4690	CCTAGTCA GGCTAGCTACAACGA AGCCTCCG	13439
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8683	AACAUCAU G CUCCUCCA	4706	TGGAGGAG GGCTAGCTACAACGA ATGATGTT	13455
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8719	UGCAUCUG G CAAAAGGG	4717	CCCTTTTG GGCTAGCTACAACGA CAGATGCA	13466
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8734	GGUGUACU A CCUCACCC	4721	GGGTGAGG GGCTAGCTACAACGA AGTACACC	13470
8739	ACUACCUC A CCCGUGAC	4722	GTCACGGG GGCTAGCTACAACGA GAGGTAGT	13471
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8746	CACCCGUG A CCCACCA	4724	TGGTGGG GGCTAGCTACAACGA CACGGGTG	13473
8751	GUGACCCC A CCACCCC	4725	GGGGGTGG GGCTAGCTACAACGA GGGGTAC	13474
8754	ACCCACCC A CCCCCCU	4726	AAGGGGGG GGCTAGCTACAACGA GGTGGGT	13475
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8765	CCCCUUG G CGGGCUGC	4728	GCAGCCCG GGCTAGCTACAACGA GCAAGGGG	13477
8769	UUGCGCG G CUGCGUGG	4729	CCACGCAG GGCTAGCTACAACGA CCGCGCAA	13478
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8774	CGGGCUG G UGGGAGAC	4731	GTCTCCA GGCTAGCTACAACGA GCAGCCCG	13480
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8784	GGGAGACA G CUAGAAGC	4733	GCTTCTAG GGCTAGCTACAACGA TGTCTCCC	13482
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8818	GCUAGGCA A CAUCAUCA	4740	TGATGATG GGCTAGCTACAACGA TGCCTAGC	13489
8820	UAGGCAAC A UCAUCAUG	4741	CATGATGA GGCTAGCTACAACGA GTTGCCTA	13490
8823	GCAACAUC A UCAUGUUU	4742	AAACATGA GGCTAGCTACAACGA GATGTTGC	13491
8826	ACAUCAUC A UGUUUGCA	4743	TGCAACA GGCTAGCTACAACGA GATGATGT	13492
8828	AUCAUCAU G UUUGCACC	4744	GGTGCAA GGCTAGCTACAACGA ATGATGAT	13493
8832	UCAUGUUU G CACCCACU	4745	AGTGGGTG GGCTAGCTACAACGA AAACATGA	13494
8834	AUGUUUUG A CCCACUCU	4746	AGAGTGGG GGCTAGCTACAACGA GCAAACAT	13495
8838	UUGCACCC A CUCUAUGG	4747	CCATAGAG GGCTAGCTACAACGA GGGTGCAA	13496
8843	CCCACUCU A UGGGUUAG	4748	CTTACCCA GGCTAGCTACAACGA AGAGTGGG	13497
8847	CUCUAUGG G UAAGGAUG	4749	CATCCTTA GGCTAGCTACAACGA CCATAGAG	13498
8853	GGGUAAGG A UGAUUCUG	4750	CAGAATCA GGCTAGCTACAACGA CCTTACCC	13499
8856	UAAGGAUG A UUCUGAUG	4751	CATCAGAA GGCTAGCTACAACGA CATCCTTA	13500
8862	UGAUUCUG A UGACUCAC	4752	GTGAGTCA GGCTAGCTACAACGA CAGAATCA	13501
8865	UUCUGAUG A CUCACUUC	4753	GAAGTGAG GGCTAGCTACAACGA CATCAGAA	13502
8869	GAUGACUC A CUUCUUCU	4754	AGAAGAAG GGCTAGCTACAACGA GAGTCATC	13503
8880	UCUUCUCC A UCCUUCUA	4755	TAGAAGGA GGCTAGCTACAACGA GGAGAAGA	13504
8889	UCCUUCUA G CCCAGGAG	4756	CTCCTGGG GGCTAGCTACAACGA TAGAAGGA	13505
8897	GCCCAGGA G CAACUUGA	4757	TCAAGTTG GGCTAGCTACAACGA TCCTGGGC	13506
8900	CAGGAGCA A CUUGAGAA	4758	TTCTCAAG GGCTAGCTACAACGA TGCTCCTG	13507
8910	UUGAGAAA G CCCUAGAC	4759	GTCTAGGG GGCTAGCTACAACGA TTTCTCAA	13508
8917	AGCCCUAG A CUGCCAGA	4760	TCTGGCAG GGCTAGCTACAACGA CTAGGGCT	13509
8920	CCUAGACU G CCAGAUUC	4761	AGATCTGG GGCTAGCTACAACGA AGTCTAGG	13510
8925	ACUGCCAG A UCUACGGG	4762	CCCGTAGA GGCTAGCTACAACGA CTGGCAGT	13511
8929	CCAGAUUC A CGGGGCUU	4763	AAGCCCCG GGCTAGCTACAACGA AGATCTGG	13512
8934	UCUACGGG G CUUGUAC	4764	GTAACAAG GGCTAGCTACAACGA CCCGTAGA	13513
8938	CGGGGCUU G UUAUCUCA	4765	TGGAGTAA GGCTAGCTACAACGA AAGCCCCG	13514
8941	GGCUUGUU A CUCCAUG	4766	CAATGGAG GGCTAGCTACAACGA AACAAGCC	13515
8946	GUUACUCC A UUGAGCCA	4767	TGGCTCAA GGCTAGCTACAACGA GGAGTAAC	13516
8951	UCCAUUGA G CCACUUGA	4768	TCAAGTGG GGCTAGCTACAACGA TCAATGGA	13517
8954	AUUGAGCC A CUUGACCU	4769	AGGTCAAG GGCTAGCTACAACGA GGCTCAAT	13518
8959	GCCACUUG A CCUACCUC	4770	GAGGTAGG GGCTAGCTACAACGA CAAGTGGC	13519
8963	CUUGACCU A CCUCAGAU	4771	ATCTGAGG GGCTAGCTACAACGA AGGTCAAG	13520

8970	UACCUCAG A UCAUUCAG	4772	CTGAATGA GGCTAGCTACAACGA CTGAGGTA	13521
8973	CUCAGAUC A UUCAGCGA	4773	TCGCTGAA GGCTAGCTACAACGA GATCTGAG	13522
8978	AUCAUUA G CGACUCCA	4774	TGGAGTCG GGCTAGCTACAACGA TGAATGAT	13523
8981	AUUCAGCG A CUCCAUGG	4775	CCATGGAG GGCTAGCTACAACGA CGCTGAAT	13524
8986	GCGACUCC A UGGUCUUA	4776	TAAGACCA GGCTAGCTACAACGA GGAGTCGC	13525
8989	ACUCCAUG G UCUUAGCG	4777	CGCTAAGA GGCTAGCTACAACGA CATGGAGT	13526
8995	UGGUCUUA G CGCAUUUU	4778	AAAATGCG GGCTAGCTACAACGA TAAGACCA	13527
8997	GUCUUAGC G CAUUUUA	4779	TGAAAATG GGCTAGCTACAACGA GCTAAGAC	13528
8999	CUUAGCGC A UUUUCACU	4780	AGTGAAAA GGCTAGCTACAACGA GCGCTAAG	13529
9005	GCAUUUUC A CUCCAUAG	4781	CTATGGAG GGCTAGCTACAACGA GAAAATGC	13530
9010	UUCACUCC A UAGUUACU	4782	AGTAAGTA GGCTAGCTACAACGA GGAGTGAA	13531
9013	ACUCCAUA G UUACUCCC	4783	GGGAGTAA GGCTAGCTACAACGA TATGGAGT	13532
9016	CCAUAGUU A CUCCCCAG	4784	CTGGGGAG GGCTAGCTACAACGA AACTATGG	13533
9025	CUCCCCAG G UGAAAUCA	4785	TGATTTCA GGCTAGCTACAACGA CTGGGGAG	13534
9030	CAGGUGAA A UCAAUAGG	4786	CCTATTGA GGCTAGCTACAACGA TTCACCTG	13535
9034	UGAAAUCA A UAGGGUGG	4787	CCACCCTA GGCTAGCTACAACGA TGATTTCA	13536
9039	UCAAUAGG G UGGCAUCA	4788	TGATGCCA GGCTAGCTACAACGA CCTATTGA	13537
9042	AUAGGGUG G CAU AUGC	4789	GCATGATG GGCTAGCTACAACGA CACCCTAT	13538
9044	AGGGUGGC A UCAUGCCU	4790	AGGCATGA GGCTAGCTACAACGA GCCACCCT	13539
9047	GUGGCAUC A UGCCUCAG	4791	CTGAGGCA GGCTAGCTACAACGA GATGCCAC	13540
9049	GGCAUCAU G CCUCAGGA	4792	TCCTGAGG GGCTAGCTACAACGA ATGATGCC	13541
9059	CUCAGGAA A CUUGGGGU	4793	ACCCCAAG GGCTAGCTACAACGA TTCCTGAG	13542
9066	AACUUGGG G UACCACCC	4794	GGGTGGTA GGCTAGCTACAACGA CCAAGTT	13543
9068	CUUGGGGU A CCACCCUU	4795	AAGGGTGG GGCTAGCTACAACGA ACCCAAG	13544
9071	GGGGUACC A CCCUUGCG	4796	CGCAAGGG GGCTAGCTACAACGA GGTACCCC	13545
9077	CCACCCUU G CGAACCUG	4797	CAGGTTTC GGCTAGCTACAACGA AAGGGTGG	13546
9081	CCUUGCGA A CCUGGAGA	4798	TCTCCAGG GGCTAGCTACAACGA TCGCAAGG	13547
9089	ACCUGGAG A CAUCGGGC	4799	GCCCGATG GGCTAGCTACAACGA CTCCAGGT	13548
9091	CUGGAGAC A UCGGGCCA	4800	TGGCCCGA GGCTAGCTACAACGA GTCTCCAG	13549
9096	GACAUCGG G CCAGAAGU	4801	ACTTCTGG GGCTAGCTACAACGA CCGATGTC	13550
9103	GGCCAGAA G UGUUCGCG	4802	CGCGAACA GGCTAGCTACAACGA TTCTGGCC	13551
9105	CCAGAAGU G UUCGCGCU	4803	AGCGCGAA GGCTAGCTACAACGA ACTTCTGG	13552
9109	AAGUGUUC G CGCUAAGC	4804	GCTTAGCG GGCTAGCTACAACGA GAACACTT	13553
9111	GUGUUCGC G CUAAGCUA	4805	TAGCTTAG GGCTAGCTACAACGA GCGAACAC	13554
9116	CGCGCUAA G CUACUGUC	4806	GACAGTAG GGCTAGCTACAACGA TTAGCGCG	13555
9119	GCUAAGCU A CUGUCCCA	4807	TGGGACAG GGCTAGCTACAACGA AGCTTAGC	13556
9122	AAGCUACU G UCCCAGGG	4808	CCCTGGGA GGCTAGCTACAACGA AGTAGCTT	13557
9138	GGGGGAGG G CCGCCACC	4809	GGTGGCGG GGCTAGCTACAACGA CCTCCCCC	13558
9141	GGAGGGCC G CCACCUGU	4810	ACAGGTGG GGCTAGCTACAACGA GGCCCTCC	13559
9144	GGGCCGCC A CCUGUGGC	4811	GCCACAGG GGCTAGCTACAACGA GGCGGCCC	13560
9148	CGCCACCU G UGGCAGGU	4812	ACCTGCCA GGCTAGCTACAACGA AGGTGGCG	13561
9151	CACCUGUG G CAGGUACC	4813	GGTACCTG GGCTAGCTACAACGA CACAGGTG	13562
9155	UGUGGCAG G UACCUCUU	4814	AAGAGGTA GGCTAGCTACAACGA CTGCCACA	13563
9157	UGGCAGGU A CCUCUUA	4815	TGAAGAGG GGCTAGCTACAACGA ACCTGCCA	13564
9166	CCUCUUA A CUGGGCAG	4816	CTGCCAG GGCTAGCTACAACGA TGAAGAGG	13565
9171	UCAACUGG G CAGUAAAG	4817	CTTTACTG GGCTAGCTACAACGA CCAGTTGA	13566
9174	ACUGGGCA G UAAAGACC	4818	GGTCTTTA GGCTAGCTACAACGA TGCCAGT	13567
9180	CAGUAAAG A CCAAACUC	4819	GAGTTTGG GGCTAGCTACAACGA CTTTACTG	13568
9185	AAGACCAA A CUCAAACU	4820	AGTTTGAG GGCTAGCTACAACGA TTGGTCTT	13569
9191	AAACUCAA A CUCACUCC	4821	GGAGTGAG GGCTAGCTACAACGA TTGAGTTT	13570
9195	UCAAAUC A CUCCAAUC	4822	GATTGGAG GGCTAGCTACAACGA GAGTTTGA	13571
9201	UCACUCCA A UCCAGCU	4823	AGCTGGGA GGCTAGCTACAACGA TGGAGTGA	13572
9207	CAAUCCCA G CUGCGUCU	4824	AGACGCAG GGCTAGCTACAACGA TGGGATTG	13573
9210	UCCAGGCU G CGUCUCAG	4825	CTGAGACG GGCTAGCTACAACGA AGCTGGGA	13574
9212	CCAGCUGC G UCUCAGUU	4826	AACTGAGA GGCTAGCTACAACGA GCAGCTGG	13575
9218	GCGUCUCA G UUGGACUU	4827	AAGTCCAA GGCTAGCTACAACGA TGAGACGC	13576

9223	UCAGUUGG A CUUGUCCA	4828	TGGACAAG GGCTAGCTACAACGA CCAACTGA	13577
9227	UUGGACUU G UCCAACUG	4829	CAGTTGGA GGCTAGCTACAACGA AAGTCCAA	13578
9232	CUUGUCCA A CUGGUUCG	4830	CGAACCAG GGCTAGCTACAACGA TGGACAAG	13579
9236	UCCAACUG G UUCGUUGC	4831	GCAACGAA GGCTAGCTACAACGA CAGTTGGA	13580
9240	ACUGGUUC G UUGCUGGC	4832	GCCAGCAA GGCTAGCTACAACGA GAACCACT	13581
9243	GGUUCGUU G CUGGCUAC	4833	GTAGCCAG GGCTAGCTACAACGA AACGAACC	13582
9247	CGUUGCUG G CUACAGCG	4834	CGCTGTAG GGCTAGCTACAACGA CAGCAACG	13583
9250	UGCUGGCU A CAGCGGGG	4835	CCCCGCTG GGCTAGCTACAACGA AGCCAGCA	13584
9253	UGGCUACA G CGGGGGAG	4836	CTCCCCCG GGCTAGCTACAACGA TGTAGCCA	13585
9262	CGGGGGAG A CGUGUAUC	4837	GATACACG GGCTAGCTACAACGA TCCCCCG	13586
9264	GGGAGAC G UGUUAUCAC	4838	GTGATACA GGCTAGCTACAACGA GTCTCCCC	13587
9266	GGAGACGU G UAUCACAG	4839	CTGTGATA GGCTAGCTACAACGA ACGTCTCC	13588
9268	AGACGUGU A UCACAGCC	4840	GGCTGTGA GGCTAGCTACAACGA ACACGTCT	13589
9271	CGUGUAUC A CAGCCUGU	4841	ACAGGCTG GGCTAGCTACAACGA GATACACG	13590
9274	GUUAUACA G CCUGUCUC	4842	GAGACAGG GGCTAGCTACAACGA TGTGATAC	13591
9278	CACAGCCU G UCUCGUGC	4843	GCACGAGA GGCTAGCTACAACGA AGGCTGTG	13592
9283	CCUGUCUC G UGCCCAG	4844	GTCGGGCA GGCTAGCTACAACGA GAGACAGG	13593
9285	UGUCUCGU G CCCGACCC	4845	GGGTCCGG GGCTAGCTACAACGA ACGAGACA	13594
9290	CGUGCCCG A CCCCGCUG	4846	CAGCGGGG GGCTAGCTACAACGA CGGGCACG	13595
9295	CCGACCCC G UGGGUUCA	4847	TGAACCAG GGCTAGCTACAACGA GGGGTCGG	13596
9299	CCCCGCUG G UUCAUGCU	4848	AGCATGAA GGCTAGCTACAACGA CAGCGGGG	13597
9303	GCUGGUUC A UGCUUUGC	4849	GCAAAGCA GGCTAGCTACAACGA GAACCACT	13598
9305	UGGUUCAU G CUUUGCCU	4850	AGGCAAAG GGCTAGCTACAACGA ATGAACCA	13599
9310	CAUGCUUU G CCUACUCC	4851	GGAGTAGG GGCTAGCTACAACGA AAAGCATG	13600
9314	CUUUGCCU A CUCCUACU	4852	AGTAGGAG GGCTAGCTACAACGA AGGCAAAG	13601
9320	CUACUCCU A CUCUCCGU	4853	ACGGAGAG GGCTAGCTACAACGA AGGAGTAG	13602
9327	UACUCCU G UAGGGGUA	4854	TACCCCTA GGCTAGCTACAACGA GGAGAGTA	13603
9333	CCGUAGGG G UAGGCAUC	4855	GATGCCTA GGCTAGCTACAACGA CCCTACGG	13604
9337	AGGGGUAG G CAUCUACC	4856	GGTAGATG GGCTAGCTACAACGA CTACCCCT	13605
9339	GGGUAGGC A UCUACCUG	4857	CAGGTAGA GGCTAGCTACAACGA GCCTACCC	13606
9343	AGGCAUCU A CCUGCUCC	4858	GGAGCAGG GGCTAGCTACAACGA AGATGCCT	13607
9347	AUCUACCU G CUCCCCAA	4859	TTGGGGAG GGCTAGCTACAACGA AGGTAGAT	13608
9355	GCUCCCCA A CCGAUGAA	4860	TTCATCGG GGCTAGCTACAACGA TGGGGAGC	13609
9359	CCCAACCG A UGAACAGG	4861	CCTGTTCA GGCTAGCTACAACGA CGGTTGGG	13610
9363	ACCGAUGA A CAGGGAGC	4862	GCTCCCTG GGCTAGCTACAACGA TCATCGGT	13611
9370	AACAGGGA G CUAACAC	4863	GTGTTTAG GGCTAGCTACAACGA TCCCTGTT	13612
9375	GGAGCUAA A CACUCCAG	4864	CTGGAGTG GGCTAGCTACAACGA TTAGCTCC	13613
9377	AGCUAAAC A CUCCAGGC	4865	GCCTGGAG GGCTAGCTACAACGA GTTTAGCT	13614
9384	CACUCCAG G CCAAUAGG	4866	CCTATTGG GGCTAGCTACAACGA CTGGAGTG	13615
9388	CCAGGCCA A UAGGCCAU	4867	ATGGCCTA GGCTAGCTACAACGA TGGCCTGG	13616
9392	GCCAAUAG G CCAUCCCG	4868	CGGGATGG GGCTAGCTACAACGA CTATTGGC	13617
9395	AAUAGGCC A UCCCGUUU	4869	AAACGGGA GGCTAGCTACAACGA GGCCTATT	13618
9400	GCCAUCCC G UUUUUUUU	4870	AAAAAAA GGCTAGCTACAACGA GGGATGGC	13619

Input Sequence = HPC1S1. Cut Site = R/Y

Arm Length = 8. Core Sequence = GGCTAGCTACAACGA

HPC1S1 Hepatitis C virus (strain HCV-1b, clone HCV-K1-S1), complete genome; acc#
gi|1030702|dbj|D50483.1; 9410 nt

Table XIX: HCV minus strand DNzyme and Substrate Sequence

Pos	Substrate	SeqID	DNzyme	SeqID
9413	AAAAAAA A CGGGAUGG	4871	CCATCCCC GGCTAGCTACAACGA TTTT	13620
9408	AAAACGGG A UGGCCUAU	4872	ATAGGCCA GGCTAGCTACAACGA CCCGTTT	13621
9405	ACGGGAUG G CCUAUUGG	4873	CCAATAGG GGCTAGCTACAACGA CATCCCGT	13622
9401	GAUGGCCU A UUGGCCUG	4874	CAGGCCAA GGCTAGCTACAACGA AGGCCATC	13623
9397	GCCUAUUG G CCUGGAGU	4875	ACTCCAGG GGCTAGCTACAACGA CAATAGGC	13624
9390	GGCCUGGA G UGUUUAGC	4876	GCTAAACA GGCTAGCTACAACGA TCCAGGCC	13625
9388	CCUGGAGU G UUUAGCUC	4877	GAGCTAAA GGCTAGCTACAACGA ACTCCAGG	13626
9383	AGUGUUUA G CUCCUGU	4878	ACAGGGAG GGCTAGCTACAACGA TAAACACT	13627
9376	AGCUCUUU G UUCAUCGG	4879	CCGATGAA GGCTAGCTACAACGA AGGGAGCT	13628
9372	CCCUGUUC A UCGGUUGG	4880	CCAACCGA GGCTAGCTACAACGA GAACAGGG	13629
9368	GUUCAUCG G UUGGGGAG	4881	CTCCCCAA GGCTAGCTACAACGA CGATGAAC	13630
9360	GUUGGGGA G CAGGUAGA	4882	TCTACCTG GGCTAGCTACAACGA TCCCAAC	13631
9356	GGGAGCAG G UAGAUGCC	4883	GGCATCTA GGCTAGCTACAACGA CTGCTCCC	13632
9352	GCAGGUAG A UGCCUACC	4884	GGTAGGCA GGCTAGCTACAACGA CTACCTGC	13633
9350	AGGUAGAU G CCUACCCC	4885	GGGGTAGG GGCTAGCTACAACGA ATCTACCT	13634
9346	AGAUGCCU A CCCCACG	4886	CGTAGGGG GGCTAGCTACAACGA AGGCATCT	13635
9340	CUACCCCU A CGGAGAGU	4887	ACTCTCCG GGCTAGCTACAACGA AGGGTAG	13636
9333	UACGGAGA G UAGGAGUA	4888	TACTCCTA GGCTAGCTACAACGA TCTCCGTA	13637
9327	GAGUAGGA G UAGGCAA	4889	TTTGCTTA GGCTAGCTACAACGA TCCTACTC	13638
9323	AGGAGUAG G CAAAGCAU	4890	ATGCTTTG GGCTAGCTACAACGA TCTCTCT	13639
9318	UAGGCAA G CAUGAAC	4891	GGTTCATG GGCTAGCTACAACGA TTTGCTTA	13640
9316	GGCAAAGC A UGAACAG	4892	CTGGTTCA GGCTAGCTACAACGA GCTTTGCC	13641
9312	AAGCAUGA A CCAGCGGG	4893	CCCGCTGG GGCTAGCTACAACGA TCATGCTT	13642
9308	AUGAACCA G CGGGGUCG	4894	CGACCCCG GGCTAGCTACAACGA TGGTTCAT	13643
9303	CCAGCGGG G UCGGGCAC	4895	GTGCCCGA GGCTAGCTACAACGA CCCGCTGG	13644
9298	GGGGUCGG G CACGAGAC	4896	GTCTCGTG GGCTAGCTACAACGA CCGACCCC	13645
9296	GGUCGGGC A CGAGACAG	4897	CTGTCTCG GGCTAGCTACAACGA GCCCGACC	13646
9291	GGCAGAG A CAGGUGU	4898	ACAGCCTG GGCTAGCTACAACGA TTCGTGCC	13647
9287	CGAGACAG G CUGUGAUA	4899	TATCACAG GGCTAGCTACAACGA CTGTCTCG	13648
9284	GACAGGCU G UGAUACAC	4900	GTGTATCA GGCTAGCTACAACGA AGCCTGTC	13649
9281	AGGCUGUG A UACACGUC	4901	GACGTGTA GGCTAGCTACAACGA CACAGCCT	13650
9279	GCUGUGAU A CACGUCUC	4902	GAGACGTG GGCTAGCTACAACGA ATCACAGC	13651
9277	UGUGAUAC A CGUCUCCC	4903	GGGAGACG GGCTAGCTACAACGA GTATCACA	13652
9275	UGAUACAC G UCUCUCCC	4904	GGGGGAGA GGCTAGCTACAACGA GTGTATCA	13653
9266	UCUCUCCC G CUGUAGCC	4905	GGCTACAG GGCTAGCTACAACGA GGGGGAGA	13654
9263	CCCCGCU G UAGCCAGC	4906	GCTGGCTA GGCTAGCTACAACGA AGCGGGGG	13655
9260	CCGCUGUA G CCAGCAAC	4907	GTTGCTGG GGCTAGCTACAACGA TACAGCGG	13656
9256	UGUAGCCA G CAACGAAC	4908	GTTCTGTTG GGCTAGCTACAACGA TGGCTACA	13657
9253	AGCCAGCA A CGAACCAG	4909	CTGGTTTCG GGCTAGCTACAACGA TGCTGGCT	13658
9249	AGCAACGA A CCAGUUGG	4910	CCAACCTG GGCTAGCTACAACGA TCGTTGCT	13659
9245	ACGAACCA G UUGGACAA	4911	TTGTCCAA GGCTAGCTACAACGA TGGTTCGT	13660
9240	CCAGUUGG A CAAGUCCA	4912	TGGACTTG GGCTAGCTACAACGA CCAACTGG	13661
9236	UUGGACAA G UCCAACUG	4913	CAGTTGGA GGCTAGCTACAACGA TTGTCCAA	13662
9231	CAAGUCCA A CUGAGACG	4914	CGTCTCAG GGCTAGCTACAACGA TGGACTTG	13663
9225	CAACUGAG A CGCAGCUG	4915	CAGCTGCG GGCTAGCTACAACGA CTCAGTTG	13664
9223	ACUGAGAC G CAGCUGGG	4916	CCCAGCTG GGCTAGCTACAACGA GTCTCAGT	13665
9220	GAGACGCA G CUGGGAUU	4917	AATCCCGA GGCTAGCTACAACGA TGCGTCTC	13666
9214	CAGCUGGG A UUGGAGUG	4918	CACTCCAA GGCTAGCTACAACGA CCCAGCTG	13667
9208	GGAUUGGA G UGAGUUUG	4919	CAAACCTA GGCTAGCTACAACGA TCCAATCC	13668
9204	UGGAGUGA G UUUGAGUU	4920	AACTCAA GGCTAGCTACAACGA TCACTCCA	13669
9198	GAGUUUGA G UUUGGUCU	4921	AGACCAA GGCTAGCTACAACGA TCAAACCT	13670

9193	UGAGUUUG G UCUUUACU	4922	AGTAAAGA GGCTAGCTACAACGA CAAACTCA	13671
9187	UGGUCUUU A CUGCCAG	4923	CTGGGCAG GGCTAGCTACAACGA AAAGACCA	13672
9184	UCUUUACU G CCCAGUUG	4924	CAACTGGG GGCTAGCTACAACGA AGTAAAGA	13673
9179	ACUGCCCA G UUGAAGAG	4925	CTCTTCAA GGCTAGCTACAACGA TGGGCAGT	13674
9170	UUGAAGAG G UACCUGCC	4926	GGCAGGTA GGCTAGCTACAACGA CTCTTCAA	13675
9168	GAAGAGGU A CCUGCCAC	4927	GTGGCAGG GGCTAGCTACAACGA ACCTCTTC	13676
9164	AGGUACCU G CCACAGGU	4928	ACCTGTGG GGCTAGCTACAACGA AGGTACCT	13677
9161	UACCUGCC A CAGGUGGC	4929	GCCACCTG GGCTAGCTACAACGA GGCAGGTA	13678
9157	UGCCACAG G UGGCGGCC	4930	GGCCGCCA GGCTAGCTACAACGA CTGTGGCA	13679
9154	CACAGGUG G CGGCCUC	4931	GAGGGCCG GGCTAGCTACAACGA CACTGTGT	13680
9151	AGGUGGCG G CCCUCCCC	4932	GGGGAGGG GGCTAGCTACAACGA CGCCACCT	13681
9135	CCCCUGGG A CAGUAGCU	4933	AGCTACTG GGCTAGCTACAACGA CCCAGGGG	13682
9132	CUGGGACA G UAGCUUAG	4934	CTAAGCTA GGCTAGCTACAACGA TGTCCCAG	13683
9129	GGACAGUA G CUUAGCGC	4935	GCGCTAAG GGCTAGCTACAACGA TACTGTCC	13684
9124	GUAGCUUA G CGCGAACA	4936	TGTTCCGC GGCTAGCTACAACGA TAAGCTAC	13685
9122	AGCUUAGC G CGAACACU	4937	AGTGTTCG GGCTAGCTACAACGA GCTAAGCT	13686
9118	UAGCGCGA A CACUUCUG	4938	CAGAAGTG GGCTAGCTACAACGA TCGCGCTA	13687
9116	GCGCGAAC A CUUCUGGC	4939	GCCAGAAG GGCTAGCTACAACGA GTTCGCGC	13688
9109	CACUUCUG G CCCGAUGU	4940	ACATCGGG GGCTAGCTACAACGA CAGAAGTG	13689
9104	CUGGCCCC G UGUCUCCA	4941	TGGAGACA GGCTAGCTACAACGA CGGGCCAG	13690
9102	GGCCCCAU G UCUCAGG	4942	CCTGGAGA GGCTAGCTACAACGA ATCGGGCC	13691
9094	GUCUCCAG G UUCGCAAG	4943	CTTGCGAA GGCTAGCTACAACGA CTGGAGAC	13692
9090	CCAGGUUC G CAAGGGUG	4944	CACCCTTG GGCTAGCTACAACGA GAACCTGG	13693
9084	UCGCAAGG G UGGUACCC	4945	GGGTACCA GGCTAGCTACAACGA CCTTGCGA	13694
9081	CAAGGGUG G UACCCCAA	4946	TTGGGGTA GGCTAGCTACAACGA CACCCTTG	13695
9079	AGGGUGGU A CCCCAAGU	4947	ACTTGGGG GGCTAGCTACAACGA ACCACCCT	13696
9072	UACCCCAA G UUUCCUGA	4948	TCAGGAAA GGCTAGCTACAACGA TTGGGGTA	13697
9062	UUCCUGAG G CAUGAUGC	4949	GCATCATG GGCTAGCTACAACGA CTCAGGAA	13698
9060	CCUGAGGC A UGAUGCCA	4950	TGGCATCA GGCTAGCTACAACGA GCCTCAGG	13699
9057	GAGGCAUG A UGCCACCC	4951	GGGTGGCA GGCTAGCTACAACGA CATGCCTC	13700
9055	GGCAUGAU G CCACCCUA	4952	TAGGGTGG GGCTAGCTACAACGA ATCATGCC	13701
9052	AUGAUGCC A CCCUAUUG	4953	CAATAGGG GGCTAGCTACAACGA GGCATCAT	13702
9047	GCCACCCU A UUGAUUUC	4954	GAAATCAA GGCTAGCTACAACGA AGGGTGGC	13703
9043	CCCUAUUG A UUUACCU	4955	AGGTGAAA GGCTAGCTACAACGA CAATAGGG	13704
9038	UUGAUUUC A CCUGGGGA	4956	TCCCCAGG GGCTAGCTACAACGA GAAATCAA	13705
9029	CCUGGGGA G UAACUAUG	4957	CATAGTTA GGCTAGCTACAACGA TCCCCAGG	13706
9026	GGGGAGUA A CUAUGGAG	4958	CTCCATAG GGCTAGCTACAACGA TACTCCCC	13707
9023	GAGUAACU A UGGAGUGA	4959	TCACTCCA GGCTAGCTACAACGA AGTTACTC	13708
9018	ACUAUGGA G UGAAAAUG	4960	CATTTTCA GGCTAGCTACAACGA TCCATAGT	13709
9012	GAGUGAAA A UGCGCUAA	4961	TTAGCGCA GGCTAGCTACAACGA TTCTACTC	13710
9010	GUGAAAAU G CGCUAAGA	4962	TCTTAGCG GGCTAGCTACAACGA ATTTTTCAC	13711
9008	GAAAAUGC G CUAAGACC	4963	GGTCTTAG GGCTAGCTACAACGA GCATTTTC	13712
9002	GCGCUAAG A CCAUGGAG	4964	CTCCATGG GGCTAGCTACAACGA CTAGCGC	13713
8999	CUAAGACC A UGGAGUCG	4965	CGACTCCA GGCTAGCTACAACGA GGTCTTAG	13714
8994	ACCAUGGA G UGCUGAA	4966	TTCAGCGA GGCTAGCTACAACGA TCCATGGT	13715
8991	AUGGAGUC G CUGAAUGA	4967	TCATTTCG GGCTAGCTACAACGA GACTCCAT	13716
8986	GUCGCUGA A UGAUCUGA	4968	TCAGATCA GGCTAGCTACAACGA TCAGCGAC	13717
8983	GCUGAAUG A UCUGAGGU	4969	ACCTCAGA GGCTAGCTACAACGA CATTCAGC	13718
8976	GAUCUGAG G UAGGUCAA	4970	TTGACCTA GGCTAGCTACAACGA CTCAGATC	13719
8972	UAGGUUAG G UCAAGUGG	4971	CCACTTGA GGCTAGCTACAACGA CTACCTCA	13720
8967	UAGGUCAA G UGGCUCAA	4972	TTGAGCCA GGCTAGCTACAACGA TTGACCTA	13721
8964	GUCAAGUG G CUCAAUGG	4973	CCATTGAG GGCTAGCTACAACGA CACTTGAC	13722
8959	GUGGCUCA A UGGAGUAA	4974	TTACTCCA GGCTAGCTACAACGA TGAGCCAC	13723
8954	UCAAUUGA G UAACAAGC	4975	GCTTGTTA GGCTAGCTACAACGA TCCATTGA	13724
8951	AUGGAGUA A CAAGCCCC	4976	GGGGCTTG GGCTAGCTACAACGA TACTCCAT	13725
8947	AGUAACAA G CCCCUGAG	4977	CTACGGGG GGCTAGCTACAACGA TTGTTACT	13726

8942	CAAGCCCC G UAGAUCUG	4978	CAGATCTA GGCTAGCTACAACGA GGGGCTTG	13727
8938	CCCCGUAG A UCUGGCAG	4979	CTGCCAGA GGCTAGCTACAACGA CTACGGGG	13728
8933	UAGAUCUG G CAGUCUAG	4980	CTAGACTG GGCTAGCTACAACGA CAGATCTA	13729
8930	AUCUGGCA G UCUAGGGC	4981	GCCCTAGA GGCTAGCTACAACGA TGCCAGAT	13730
8923	AGUCUAGG G CUUUCUCA	4982	TGAGAAAG GGCTAGCTACAACGA CCTAGACT	13731
8913	UUUCUCAA G UUGCUCU	4983	AGGAGCAA GGCTAGCTACAACGA TTGAGAAA	13732
8910	CUCAAGUU G CUCCUGGG	4984	CCCAGGAG GGCTAGCTACAACGA AACTTGAG	13733
8902	GUCCUGG G CUAGAAGG	4985	CCTTCTAG GGCTAGCTACAACGA CCAGGAGC	13734
8893	CUAGAAGG A UGGAGAAG	4986	CTTCTCCA GGCTAGCTACAACGA CCTTCTAG	13735
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8878	AGAAGUGA G UCAUCAGA	4988	TCTGATGA GGCTAGCTACAACGA TCACTTCT	13737
8875	AGUGAGUC A UCAGAAUC	4989	GATTCTGA GGCTAGCTACAACGA GACTCACT	13738
8869	UCAUCAGA A UCAUCCUU	4990	AAGGATGA GGCTAGCTACAACGA TCTGATGA	13739
8866	UCAGAAUC A UCCUUACC	4991	GGTAAGGA GGCTAGCTACAACGA GATTCTGA	13740
8860	UCAUCCUU A CCCAUAGA	4992	TCTATGGG GGCTAGCTACAACGA AAGGATGA	13741
8856	CCUUAACC A UAGAGUGG	4993	CCACTCTA GGCTAGCTACAACGA GGGTAAGG	13742
8851	CCCAUAGA G UGGGUGCA	4994	TGCATCCA GGCTAGCTACAACGA TCTATGGG	13743
8847	UAGAGUGG G UGCAACA	4995	TGTTTGCA GGCTAGCTACAACGA CCACTCTA	13744
8845	GAGUGGGU G CAAACAUG	4996	CATGTTTG GGCTAGCTACAACGA ACCCACTC	13745
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8839	GUGCAAAC A UGAUGAUG	4998	CATCATCA GGCTAGCTACAACGA GTTTCAC	13747
8836	CAAACAUG A UGAUGUUG	4999	CAACATCA GGCTAGCTACAACGA CATGTTTG	13748
8833	ACAUGAUG A UGUUGCCU	5000	AGGCAACA GGCTAGCTACAACGA CATCATGT	13749
8831	AUGAUGAU G UUGCCUAG	5001	CTAGGCAA GGCTAGCTACAACGA ATCATCAT	13750
8828	AUGAUGUU G CCUAGCCA	5002	TGGCTAGG GGCTAGCTACAACGA AACATCAT	13751
8823	GUUGCCUA G CCAGGAGU	5003	ACTCCTGG GGCTAGCTACAACGA TAGGCAAC	13752
8816	AGCCAGGA G UUGACUGG	5004	CCAGTCAA GGCTAGCTACAACGA TCCTGGCT	13753
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8806	UGACUGGA G UGCUUCUA	5006	TAGAAGCA GGCTAGCTACAACGA TCCAGTCA	13755
8804	ACUGGAGU G CUUCUAGC	5007	GCTAGAAG GGCTAGCTACAACGA ACTCCAGT	13756
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8794	UUCUAGCU G UCUCCAC	5009	GTGGGAGA GGCTAGCTACAACGA AGCTAGAA	13758
8787	UGUCUCCC A CGCAGCCC	5010	GGGCTGCG GGCTAGCTACAACGA GGGAGACA	13759
8785	UCUCCAC G CAGCCGC	5011	GCGGGCTG GGCTAGCTACAACGA GTGGGAGA	13760
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8776	CAGCCCGC G CAAGGGGG	5014	CCCCCTTG GGCTAGCTACAACGA GCGGGCTG	13763
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8744	GUGAGGUA G UACACCCU	5021	AGGGTGTA GGCTAGCTACAACGA TACCTCAC	13770
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8718	UGCAUCGU G UGCAACUG	5029	CAGTTGCA GGCTAGCTACAACGA ACGATGCA	13778
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8689	AGCAUGAU G UUAUCAAC	5038	GTTGATAA GGCTAGCTACAACGA ATCATGCT	13787
8686	AUGAUGUU A UCAACUCC	5039	GGAGTTGA GGCTAGCTACAACGA AACATCAT	13788
8682	UGUUAUCA A CUCCAAGU	5040	ACTTGGAG GGCTAGCTACAACGA TGATAACA	13789
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8106	UUUCUCGC A CACACGAA	5176	TTCTGTGT GGCTAGCTACAACGA GCCAGAAA	13925
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8038	CUGGUUGG A CGCAGAAA	5190	TTTCTGCG GGCTAGCTACAACGA CCAACCAG	13939
8036	GGUUGGAC G CAGAAAC	5191	GTTTTCTG GGCTAGCTACAACGA GTCCAACC	13940
8029	CGCAGAAA A CCUCAUUU	5192	AAATGAGG GGCTAGCTACAACGA TTTCTGCG	13941
8024	AAAACCUC A UUUUUUGC	5193	GCAAAAAA GGCTAGCTACAACGA GAGGTTTT	13942
8017	CAUUUUUU G CCAUGAUG	5194	CATCATGG GGCTAGCTACAACGA AAAAAATG	13943
8014	UUUUUGCC A UGAUGGUG	5195	CACCATCA GGCTAGCTACAACGA GGCAAAAA	13944
8011	UUGCCAUG A UGGUGGUA	5196	TACCACCA GGCTAGCTACAACGA CATGGCAA	13945
8008	CCAUGAUG G UGGUAUCA	5197	TGATACCA GGCTAGCTACAACGA CATCATGG	13946
8005	UGAUGGUG G UAUCAAUU	5198	AATTGATA GGCTAGCTACAACGA CACCATCA	13947
8003	AUGGUGGU A UCAAUUGG	5199	CCAATTGA GGCTAGCTACAACGA ACCACCAT	13948
7999	UGGUAUCA A UUGGUGUC	5200	GACACCAA GGCTAGCTACAACGA TGATACCA	13949
7995	AUCAAUUG G UGUCUCAG	5201	CTGAGACA GGCTAGCTACAACGA CAATTGAT	13950

7993	CAAUUGGU G UCUCAGUG	5202	CACTGAGA GGCTAGCTACAACGA ACCAATTG	13951
7987	GUGUCUCA G UGUCUCC	5203	GGAAGACA GGCTAGCTACAACGA TGAGACAC	13952
7985	GUCUCAGU G UCUCACAG	5204	CTGGAAGA GGCTAGCTACAACGA ACTGAGAC	13953
7977	GUCUCCA G CAAGUCCU	5205	AGGACTTG GGCTAGCTACAACGA TGGAAGAC	13954
7973	UCCAGCAA G UCCUCCA	5206	TGGAAGGA GGCTAGCTACAACGA TTGCTGGA	13955
7965	GUCCUCC A CACGAGC	5207	GCTCCGTG GGCTAGCTACAACGA GGAAGGAC	13956
7963	CCUCCAC A CGGAGCGG	5208	CCGCTCCG GGCTAGCTACAACGA GTGAAGG	13957
7958	CACACGGA G CGGAUGUG	5209	CACATCCG GGCTAGCTACAACGA TCCGTGTG	13958
7954	CGGAGCGG A UGUGGUUG	5210	CAACCACA GGCTAGCTACAACGA CCGCTCCG	13959
7952	GAGCGGAU G UGGUUGAC	5211	GTCAACCA GGCTAGCTACAACGA ATCCGCTC	13960
7949	CGGAUGUG G UUGACGGC	5212	GCCGTCOA GGCTAGCTACAACGA CACATCCG	13961
7945	UGUGGUUG A CGGCCCGG	5213	CGGGGCGG GGCTAGCTACAACGA CAACCACA	13962
7942	GGUUGACG G CCCCGCUG	5214	CAGCGGGG GGCTAGCTACAACGA CGTCAACC	13963
7937	ACGGCCCC G CUGGAUAG	5215	CTATCCAG GGCTAGCTACAACGA GGGCCGT	13964
7932	CCCGCUGG A UAGGUUCC	5216	GGAACCTA GGCTAGCTACAACGA CCAGCGGG	13965
7928	CUGGAUAG G UCCCGGAC	5217	GTCCGGAA GGCTAGCTACAACGA CTATCCAG	13966
7921	GGUCCCGG A CGUCCUUU	5218	AAAGGACG GGCTAGCTACAACGA CCGGAACC	13967
7919	UCCCGGAC G UCCUUUGC	5219	GCAACGA GGCTAGCTACAACGA GTCCGGAA	13968
7912	CGUCCUUU G CCCCAUAA	5220	TTATGGGG GGCTAGCTACAACGA AAGGACG	13969
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7881	GGCCGAU G UGGGGCGG	5227	CGCCCCA GGCTAGCTACAACGA ATTCGGCC	13976
7875	AUGUGGGG G CGUCAGUC	5228	GACTGACG GGCTAGCTACAACGA CCCCACAT	13977
7873	GUGGGGGG G UCAGUCUG	5229	CAGACTGA GGCTAGCTACAACGA GCCCCAC	13978
7869	GGGCGUCA G UCUGCAGG	5230	CCTGCAGA GGCTAGCTACAACGA TGACGCC	13979
7865	GUCAGUCU G CAGGCUUC	5231	GAAGCCTG GGCTAGCTACAACGA AGACTGAC	13980
7861	GUCUGCAG G CUUCCUCU	5232	AGAGGAAG GGCTAGCTACAACGA CTGCAGAC	13981
7852	CUUCCUCU A CGGAUAGA	5233	TCTATCCG GGCTAGCTACAACGA AGAGGAAG	13982
7848	CUCUACGG A UAGAAGUU	5234	AACTTCTA GGCTAGCTACAACGA CCGTAGAG	13983
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7828	CCUUAACU G UGGACGCC	5238	GGCGTCCA GGCTAGCTACAACGA AGTTAAGG	13987
7824	AACUGUGG A CGCCUUCG	5239	CGAAGGCG GGCTAGCTACAACGA CCACAGTT	13988
7822	CUGUGGAC G CCUUCGCC	5240	GGCGAAGG GGCTAGCTACAACGA GTCCACAG	13989
7816	ACGCCUUC G CCUUCAUC	5241	GATGAAGG GGCTAGCTACAACGA GAAGGCGT	13990
7810	UCGCCUUC A UCUCUUG	5242	CAAGGAGA GGCTAGCTACAACGA GAAGGCGA	13991
7800	CUCCUUGA G CAGUCCC	5243	GGGACGTG GGCTAGCTACAACGA TCAAGGAG	13992
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7796	UUGAGCAC G UCCCGGUA	5245	TACCGGGA GGCTAGCTACAACGA GTGCTCAA	13994
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7787	UCCCGGUA G UGGUCGUC	5247	GACGACCA GGCTAGCTACAACGA TACCGGGA	13996
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7767	GACUUGCA G UCUGCAA	5252	TTGACAGA GGCTAGCTACAACGA TGCAAGTC	14001
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7743	CUUCUUCU G CCGCUGGC	5256	GCCAGCGG GGCTAGCTACAACGA AGAAGAAG	14005
7740	CUUCUGCC G CUGGCUUG	5257	CAAGCCAG GGCTAGCTACAACGA GGCAGAAG	14006

7736	UGCCGCUG G CUUGCGCU	5258	AGCGCAAG GGCTAGCTACAACGA CAGCGGCA	14007
7732	GCUGGCUU G CGCUGCGA	5259	TCGCAGCG GGCTAGCTACAACGA AAGCCAGC	14008
7730	UGGCUUGC G CUGCGAGA	5260	TCTCGCAG GGCTAGCTACAACGA GCAAGCCA	14009
7727	CUUGCGCU G CGAGAUGU	5261	ACATCTCG GGCTAGCTACAACGA AGCGCAAG	14010
7722	GCUGCGAG A UGUUGUAG	5262	CTACAACA GGCTAGCTACAACGA CTCGCAGC	14011
7720	UGCGAGAU G UUGUAGCG	5263	CGCTACAA GGCTAGCTACAACGA ATCTCGCA	14012
7717	GAGAUGUU G UAGCGUAG	5264	CTACGCTA GGCTAGCTACAACGA AACATCTC	14013
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7700	ACCAUGUU G UGGUGACG	5270	CGTCACCA GGCTAGCTACAACGA AACATGGT	14019
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7694	UUGUGGUG A CGCAGCAA	5272	TTGCTGCG GGCTAGCTACAACGA CACCACAA	14021
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7682	AGCAAAGA G UUGCUCAA	5275	TTGAGCAA GGCTAGCTACAACGA TCTTTGCT	14024
7679	AAAGAGUU G CUCAACGC	5276	GCGTTGAG GGCTAGCTACAACGA AACTCTTT	14025
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7506	AAGGGGGG G CAUAGAGG	5316	CCTCTATG GGCTAGCTACAACGA CCCCCTTT	14065
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7063	CGCGAGUG A UGUUACCG	5411	CGGTAAAC GGCTAGCTACAACGA CACTCGCG	14160
7061	CGAGUGAU G UUACCGCC	5412	GGCGGTAA GGCTAGCTACAACGA ATCACTCG	14161
7058	GUGAUGUU A CCGCCCAU	5413	ATGGGCGG GGCTAGCTACAACGA AACATCAC	14162
7055	AUGUUAAC G CCCAUCUC	5414	GAGATGGG GGCTAGCTACAACGA GGTAACAT	14163
7051	UACCGCCC A UCUCUGC	5415	GCAGGAGA GGCTAGCTACAACGA GGGCGGTA	14164
7044	CAUCUCCU G CCGCCACA	5416	TGTGGCGG GGCTAGCTACAACGA AGGAGATG	14165
7041	CUCCUGCC G CCACAGGA	5417	TCCTGTGG GGCTAGCTACAACGA GGCAGGAG	14166
7038	CUGCCGCC A CAGGAGGU	5418	ACCTCCTG GGCTAGCTACAACGA GGCAGGAG	14167
7031	CACAGGAG G UUGGCCUC	5419	GAGGCCAA GGCTAGCTACAACGA CTCCTGTG	14168
7027	GGAGGUUG G CCUCGAUG	5420	CATCGAGG GGCTAGCTACAACGA CAACCTCC	14169
7021	UGGCCUCG A UGAGGUCA	5421	TGACCTCA GGCTAGCTACAACGA CGAGGCCA	14170
7016	UCGAUGAG G UCAAAGUC	5422	GACTTTGA GGCTAGCTACAACGA CTCATCGA	14171
7010	AGGUCAAA G UCUGGGGA	5423	TCCCCAGA GGCTAGCTACAACGA TTTGACCT	14172
7001	UCUGGGGA G UCAUAUUG	5424	CAATATGA GGCTAGCTACAACGA TCCCCAGA	14173
6998	GGGGAGUC A UAUUGGGU	5425	ACCCAATA GGCTAGCTACAACGA GACTCCCC	14174

6996	GGAGUCAU A UUGGGUAA	5426	TTACCCAA GGCTAGCTACAACGA ATGACTCC	14175
6991	CAUAUUGG G UAAUGUAU	5427	ATACATTA GGCTAGCTACAACGA CCAATATG	14176
6988	AUUGGGUA A UGUUUGUC	5428	GACATACA GGCTAGCTACAACGA TACCCAAT	14177
6986	UGGGUAAU G UAUGUCGC	5429	GCGACATA GGCTAGCTACAACGA ATTACCCA	14178
6984	GGUAAUGU A UGUCGCCU	5430	AGGCGACA GGCTAGCTACAACGA ACATTACC	14179
6982	UAAUGUAU G UCGCCUUC	5431	GAAGGCGA GGCTAGCTACAACGA ATACATTA	14180
6979	UGUAUGUC G CCUUCGAA	5432	TTCGAAGG GGCTAGCTACAACGA GACATACA	14181
6966	CGAAGAAG G CGCAGACA	5433	TGTCTGCG GGCTAGCTACAACGA CTTCTTCG	14182
6964	AAGAAGGC G CAGACAGC	5434	GCTGTCTG GGCTAGCTACAACGA GCCTTCTT	14183
6960	AGGCGCAG A CAGCUGGC	5435	GCCAGCTG GGCTAGCTACAACGA CTGCGCCT	14184
6957	CGCAGACA G CUGGCUAG	5436	CTAGCCAG GGCTAGCTACAACGA TGTCTGCG	14185
6953	GACAGCUG G CUAGCUGA	5437	TCAGCTAG GGCTAGCTACAACGA CAGCTGTC	14186
6949	GCUGGCUA G CUGAGGAG	5438	CTCCTCAG GGCTAGCTACAACGA TAGCCAGC	14187
6941	GCUGAGGA G CUGGCCAA	5439	TTGGCCAG GGCTAGCTACAACGA TCCTCAGC	14188
6937	AGGAGCUG G CCAAGGAG	5440	CTCCTTGG GGCTAGCTACAACGA CAGCTCCT	14189
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6913	ACCCCCUG G CCAGCCUA	5442	TAGGCTGG GGCTAGCTACAACGA CAGGGGGT	14191
6909	CCUGGCCA G CCUACGCU	5443	AGCGTAGG GGCTAGCTACAACGA TGGCCAGG	14192
6905	GCCAGCCU A CGCUUAGC	5444	GCTAAGCG GGCTAGCTACAACGA AGGCTGGC	14193
6903	CAGCCUAC G CUUAGCCG	5445	CGGCTAAG GGCTAGCTACAACGA GTAGGCTG	14194
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6895	GCUUAGCC G UCUCUCCU	5447	AGGAGAGA GGCTAGCTACAACGA GGCTAAGC	14196
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6883	CUCUGUA A UGUGGGAG	5449	CTCCCACA GGCTAGCTACAACGA TACAGGAG	14198
6881	CCUGUAAU G UGGGAGGG	5450	CCCTCCCA GGCTAGCTACAACGA ATTACAGG	14199
6872	UGGGAGGG G UCGGUGAG	5451	CTCACCGA GGCTAGCTACAACGA CCCTCCCA	14200
6868	AGGGGUCG G UGAGCAUG	5452	CATGCTCA GGCTAGCTACAACGA CGACCCCT	14201
6864	GUCGGUGA G CAUGGACG	5453	CGTCCATG GGCTAGCTACAACGA TCACCGAC	14202
6862	CGGUGAGC A UGGACGUG	5454	CACGTCCA GGCTAGCTACAACGA GCTCACCG	14203
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6856	GCAUGGAC G UGAGCACU	5456	AGTGCTCA GGCTAGCTACAACGA GTCCATGC	14205
6852	GGACGUGA G CACUGCUA	5457	TAGCAGTG GGCTAGCTACAACGA TCACGTCC	14206
6850	ACGUGAGC A CUGCUACA	5458	TGTAGCAG GGCTAGCTACAACGA GCTCACGT	14207
6847	UGAGCACU G CUACAUC	5459	GGATGTAG GGCTAGCTACAACGA AGTGCTCA	14208
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6842	ACUGCUAC A UCCGGUUC	5461	GAACCGGA GGCTAGCTACAACGA GTAGCAGT	14210
6837	UACAUCCG G UUCGGGCU	5462	AGCCCCGA GGCTAGCTACAACGA CGGATGTA	14211
6831	CGGUUCGG G CUCGCAUG	5463	CATGCGAG GGCTAGCTACAACGA CCGAACCG	14212
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6825	GGGCUCGC A UGGGAGCU	5465	AGCTCCCA GGCTAGCTACAACGA GCGAGCCC	14214
6819	GCAUGGGA G CUGUGACC	5466	GGTCACAG GGCTAGCTACAACGA TCCCATGC	14215
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6803	CCAACCAG G UAUUGGUU	5470	AACCAATA GGCTAGCTACAACGA CTGGTTGG	14219
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6778	CCUGGAAU G UGACCUC	5476	GGAGGTCA GGCTAGCTACAACGA ATTCCAGG	14225
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6752	AGAGGUCC A CACGCCGG	5480	CCGGCGTG GGCTAGCTACAACGA GGACCTCT	14229
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6740	GCCGGAGC G UUUUCUGUG	5484	CACAGAAA GGCTAGCTACAACGA GTCCTGGC	14233
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6728	CUGUGCAG G CGUACCCC	5487	GGGGTACG GGCTAGCTACAACGA CTGCACAG	14236
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6724	GCAGGCGU A CCCCAUCC	5489	GGATGGGG GGCTAGCTACAACGA ACGCTGC	14238
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6677	UGGCACGG G CAUUUUAC	5498	GTAAAATG GGCTAGCTACAACGA CCGTGCCA	14247
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6668	CAUUUUAC G UUGUCAGU	5501	ACTGACAA GGCTAGCTACAACGA GTAAAATG	14250
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6653	GUGGUCAU G CCCGUCAC	5506	GTGACGGG GGCTAGCTACAACGA ATGACCAC	14255
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6646	UGCCCUGC A CGUAGUGG	5508	CCACTACG GGCTAGCTACAACGA GACGGGCA	14257
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6641	GUCACGUA G UGGAAAU	5510	GATTTCCA GGCTAGCTACAACGA TACGTGAC	14259
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6158	GCCGUGC G UCGCUCUC	5631	GAGAGCGA GGCTAGCTACAACGA GCAGCGGC	14380
6155	GCUGCGUC G CUCUCAGG	5632	CCTGAGAG GGCTAGCTACAACGA GACGCAGC	14381
6147	GCUCUCAG G CACAUAGU	5633	ACTATGTG GGCTAGCTACAACGA CTGAGAGC	14382
6145	UCUCAGGC A CAUAGUGC	5634	GCACTATG GGCTAGCTACAACGA GCCTGAGA	14383
6143	UCAGGCAC A UAGUGCGU	5635	ACGCACTA GGCTAGCTACAACGA GTGCCTGA	14384
6140	GGCACAU A UGCGUGG	5636	CCCACGA GGCTAGCTACAACGA TATGTGCC	14385
6138	CACAUAGU G CGUGGGGG	5637	CCCCCAGG GGCTAGCTACAACGA ACTATGTG	14386
6136	CAUAGUGC G UGGGGGAG	5638	CTCCCCCA GGCTAGCTACAACGA GCACTATG	14387
6127	UGGGGGAG A CAUGGUUG	5639	CAACCATG GGCTAGCTACAACGA CTCCCCCA	14388
6125	GGGGAGAC A UGGUUGCC	5640	GGCAACCA GGCTAGCTACAACGA GTCTCCCC	14389
6122	GAGACAUG G UUGCCCCG	5641	CGGGGCAA GGCTAGCTACAACGA CATGTCTC	14390
6119	ACAUGGUU G CCCC CGCA	5642	TCGCGGGG GGCTAGCTACAACGA AACCATGT	14391
6114	GUUGCCCC G CGAAGCGA	5643	TCGCTTCG GGCTAGCTACAACGA GGGGCAAC	14392
6109	CCCGCGAA G CGAACGCU	5644	AGCGTTTC GGCTAGCTACAACGA TTCGCGGG	14393
6105	CGAAGCGA A CGCUAUCA	5645	TGATAGCG GGCTAGCTACAACGA TCGTTCG	14394
6103	AAGCGAAC G CUAUCAGC	5646	GCTGATAG GGCTAGCTACAACGA GTTCGCTT	14395
6100	CGAACGCU A UCAGCCGA	5647	TCGGCTGA GGCTAGCTACAACGA AGCGTTCG	14396
6096	CGCUAUCA G CCGAUUCA	5648	TGAATCGG GGCTAGCTACAACGA TGATAGCG	14397
6092	AUCAGCCG A UUCAUCCA	5649	TGGATGAA GGCTAGCTACAACGA CGGCTGAT	14398

6088	GCCGAUUC A UCCACUGC	5650	GCAGTGGG GGCTAGCTACAACGA GAATCGGC	14399
6084	AUUCAUCC A CUGCACAG	5651	CTGTGCAG GGCTAGCTACAACGA GGATGAAT	14400
6081	CAUCCACU G CACAGCGC	5652	GCGCTGTG GGCTAGCTACAACGA AGTGGATG	14401
6079	UCCACUGC A CAGCGCCC	5653	GGGCGCTG GGCTAGCTACAACGA GCAGTGGG	14402
6076	ACUGCACA G CGCCUCU	5654	AGAGGGCG GGCTAGCTACAACGA TGTGCAGT	14403
6074	UGCACAGC G CCCUCUCC	5655	GGAGAGGG GGCTAGCTACAACGA GCTGTGCA	14404
6062	UCUCCUGG G CCCACAUG	5656	CATGTGGG GGCTAGCTACAACGA CCAGGAGA	14405
6058	CUGGGGCC A CAUGCCGA	5657	TCGGCATG GGCTAGCTACAACGA GGGCCAG	14406
6056	GGGCCAC A UGCCGACG	5658	CGTCGGCA GGCTAGCTACAACGA GTGGGGCC	14407
6054	GCCCACAU G CCGACGCA	5659	TGCGTCGG GGCTAGCTACAACGA ATGTGGGC	14408
6050	ACAUGCCG A CGCAGUAU	5660	ATACTGCG GGCTAGCTACAACGA CGGCATGT	14409
6048	AUGCCGAC G CAGUAUCG	5661	CGATACTG GGCTAGCTACAACGA GTCGGCAT	14410
6045	CCGACGCA G UAUCGUG	5662	CAGCGATA GGCTAGCTACAACGA TGCCTGG	14411
6043	GACGCAGU A UCGCUGCG	5663	CGCAGCGA GGCTAGCTACAACGA ACTGCGTC	14412
6040	GCAGUAUC G CUGCGCAC	5664	GTGCGCAG GGCTAGCTACAACGA GATACTGC	14413
6037	GUAUCGCU G CGCACACC	5665	GGTGTGCG GGCTAGCTACAACGA AGCGATAC	14414
6035	AUCGUGC G CACACCAC	5666	GTGGTGTG GGCTAGCTACAACGA GCAGCGAT	14415
6033	CGCUGCGC A CACCACCC	5667	GGTGTGTG GGCTAGCTACAACGA GCGCAGCG	14416
6031	CUGCGCAC A CCACCCCG	5668	CGGGGTGG GGCTAGCTACAACGA GTCGCGAG	14417
6028	CGCACACC A CCCCACG	5669	CGTCGGGG GGCTAGCTACAACGA GGTGTGCG	14418
6022	CCACCCCG A CGACCAGG	5670	CCTGGTCG GGCTAGCTACAACGA CGGGGTGG	14419
6019	CCCCGACG A CCAGGGCG	5671	CGCCCTGG GGCTAGCTACAACGA CGTCGGGG	14420
6013	CGACCAGG G CGCCAGGA	5672	TCCTGGCG GGCTAGCTACAACGA CCTGGTCG	14421
6011	ACCAGGGG G CCAGGAGA	5673	TCTCTGGG GGCTAGCTACAACGA GCCTGGT	14422
5998	GAGAGAGG A UGGCAGGG	5674	CCCTGCCA GGCTAGCTACAACGA CCTCTCTC	14423
5995	AGAGGAUG G CAGGGAGU	5675	ACTCCCTG GGCTAGCTACAACGA CATCCTCT	14424
5988	GGCAGGGA G UAAGUUGA	5676	TCAACTTA GGCTAGCTACAACGA TCCCTGCC	14425
5984	GGGAGUAA G UUGACCAG	5677	CTGGTCAA GGCTAGCTACAACGA TTACTCCC	14426
5980	GUAAGUUG A CCAGGUCC	5678	GGACCTGG GGCTAGCTACAACGA CAACTTAC	14427
5975	UUGACCAG G UCCUCGGU	5679	ACCGAGGA GGCTAGCTACAACGA CTGGTCAA	14428
5968	GGUCCUCG G UAGAAGGC	5680	GCCTTCTA GGCTAGCTACAACGA CGAGGACC	14429
5961	GGUAGAAG G CAUCUCCC	5681	GGGAGATG GGCTAGCTACAACGA CTTCTACC	14430
5959	UAGAAGGC A UCUCCCCG	5682	CGGGGAGA GGCTAGCTACAACGA GCCTTCTA	14431
5951	AUCUCCCC G CUCAUGAC	5683	GTCATGAG GGCTAGCTACAACGA GGGGAGAT	14432
5947	CCCCGCUC A UGACCUUG	5684	CAAGGTCA GGCTAGCTACAACGA GAGCGGGG	14433
5944	CGCUCAUG A CCUUGAAG	5685	CTTCAAGG GGCTAGCTACAACGA CATGAGCG	14434
5935	CCUUGAAG G CCACGAGA	5686	TCTCGTGG GGCTAGCTACAACGA CTTCAAGG	14435
5932	UGAAGGCC A CGAGAGCA	5687	TGCTCTCG GGCTAGCTACAACGA GGCCTTCA	14436
5926	CCACGAGA G CACCCGCC	5688	GGCGGGTG GGCTAGCTACAACGA TCTCGTGG	14437
5924	ACGAGAGC A CCCGCCAC	5689	GTGGCGGG GGCTAGCTACAACGA GCTCTCGT	14438
5920	GAGCACCC G CCACUCCU	5690	AGGAGTGG GGCTAGCTACAACGA GGGTGCTC	14439
5917	CACCCGCC A CUCCUGCU	5691	AGCAGGAG GGCTAGCTACAACGA GGCGGGTG	14440
5911	CCACUCCU G CUCCAUAG	5692	CTATGGAG GGCTAGCTACAACGA AGGAGTGG	14441
5906	CCUGCUCC A UAGCCCGC	5693	GCGGGCTA GGCTAGCTACAACGA GGAGCAGG	14442
5903	GUCCAUUA G CCCGCCAG	5694	CTGGCGGG GGCTAGCTACAACGA TATGGAGC	14443
5899	CAUAGCCC G CCAGAAUG	5695	CATTCTGG GGCTAGCTACAACGA GGGCTATG	14444
5893	CCGCCAGA A UGUCUACA	5696	TGTAGACA GGCTAGCTACAACGA TCTGGCGG	14445
5891	GCCAGAAU G UCUACAAG	5697	CTTGTTAG GGCTAGCTACAACGA ATTCTGGC	14446
5887	GAAUGUCU A CAAGCACC	5698	GGTGCTTG GGCTAGCTACAACGA AGACATTG	14447
5883	GUUAACAA G CACCUUCC	5699	GGAAGGTG GGCTAGCTACAACGA TTGTAGAC	14448
5881	CUACAAGC A CCUCCCA	5700	TGGGAAGG GGCTAGCTACAACGA GCTTGTAG	14449
5870	UUCCCAAG G CCUAUGCU	5701	AGCATAGG GGCTAGCTACAACGA CTTGGGAA	14450
5866	CAAGGCCU A UGCUGCCA	5702	TGGCAGCA GGCTAGCTACAACGA AGGCCTTG	14451
5864	AGGCCUAU G CUGCCAAC	5703	GTTGGCAG GGCTAGCTACAACGA ATAGGCCT	14452
5861	CCUAUGCU G CCAACAGC	5704	GCTGTTGG GGCTAGCTACAACGA AGCATAGG	14453
5857	UGCUGCCA A CAGCCGCG	5705	CGCGGCTG GGCTAGCTACAACGA TGGCAGCA	14454

5854	UGCCAACA G CCGCGCCA	5706	TGGCGCGG GGCTAGCTACAACGA TGTGGCA	14455
5851	CAACAGCC G CGCCAGCG	5707	CGCTGGCG GGCTAGCTACAACGA GGCTGTTG	14456
5849	ACAGCCGC G CCAGCGAU	5708	ATCGCTGG GGCTAGCTACAACGA GCGGCTGT	14457
5845	CCGCGCCA G CGAUGCCG	5709	CGGCATCG GGCTAGCTACAACGA TGGCGCGG	14458
5842	CGCCAGCG A UGCCGGCG	5710	CGCCGGCA GGCTAGCTACAACGA CGCTGGCG	14459
5840	CCAGCGAU G CCGCGGCC	5711	GGCGCCGG GGCTAGCTACAACGA ATCGCTGG	14460
5836	CGAUGCCG G CGCCACG	5712	CGTGGGCG GGCTAGCTACAACGA CGGCATCG	14461
5834	AUGCCGGC G CCCACGAA	5713	TTCGTGGG GGCTAGCTACAACGA GCCGCGCAT	14462
5830	CGGCGCCC A CGAAGGCC	5714	GGCCTTCG GGCTAGCTACAACGA GGGCGCCG	14463
5824	CCACGAAG G CCGAAACG	5715	CGTTTCGG GGCTAGCTACAACGA TTCTGTGG	14464
5818	AGGCCGAA A CGGCUCUG	5716	CAGAGCCG GGCTAGCTACAACGA TTCGGCCT	14465
5815	CCGAAACG G CUCUGGGG	5717	CCCCAGAG GGCTAGCTACAACGA CGTTTCGG	14466
5803	UGGGGGGA G CGAGUUGG	5718	CCAACTCG GGCTAGCTACAACGA TCCCCCA	14467
5799	GGGAGCGA G UUGGGCGG	5719	CCGCCAA GGCTAGCTACAACGA TCGCTCCC	14468
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5791	GUUGGGCG G CCACCCAC	5721	GTGGGTGG GGCTAGCTACAACGA CGCCCAAC	14470
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5784	GGCCAGCC A CCCUCCA	5723	TGGGAGGG GGCTAGCTACAACGA GGTGGGCC	14472
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5771	CCCAAGAU G UUGAACAG	5725	CTGTTCAA GGCTAGCTACAACGA ATCTTGGG	14474
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5758	ACAGGAGG G UGUUUGG	5727	CCAAAGCA GGCTAGCTACAACGA CCTCTGT	14476
5756	AGGAGGGU G CUUUGGGU	5728	ACCCAAAG GGCTAGCTACAACGA ACCCTCCT	14477
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5746	UUUGGGUG G UGAGCGGG	5730	CCCCTCA GGCTAGCTACAACGA CACCCAAA	14479
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5731	GGCUGGUG A UGGAGGCU	5734	AGCCTCCA GGCTAGCTACAACGA CACCAGCC	14483
5725	UGAUGGAG G CUGUGAAU	5735	ATTCACAG GGCTAGCTACAACGA CTCCATCA	14484
5722	UGGAGGCU G UGAAUGCC	5736	GGCATTCA GGCTAGCTACAACGA AGCCTCCA	14485
5718	GGCUGUGA A UGCCAUCA	5737	TGATGGCA GGCTAGCTACAACGA TCACAGCC	14486
5716	CUGUGAAU G CCAUCAAU	5738	ATTGATGG GGCTAGCTACAACGA ATTCACAG	14487
5713	UGAAUGCC A UCAAUGAU	5739	ATCATTGA GGCTAGCTACAACGA GGCATTCA	14488
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5704	UCAAUAGU G CUAUCGCG	5742	CGCGATAG GGCTAGCTACAACGA ATCATTGA	14491
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5698	AUGCUAUC G CGGGGUUC	5744	GAACCCCG GGCTAGCTACAACGA GATAGCAT	14493
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5685	GUUCCAG G CAGAGUGG	5746	CCACTCTG GGCTAGCTACAACGA CTGGGAAC	14495
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5676	CAGAGUGG A CAAGCCUG	5748	CAGGCTTG GGCTAGCTACAACGA CCACTCTG	14497
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5668	ACAAGCCU G CUAGGUAC	5750	GTACCTAG GGCTAGCTACAACGA AGGCTTGT	14499
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5656	GGUACUGU A UCCCGCUG	5754	CAGCGGGA GGCTAGCTACAACGA ACAGTACC	14503
5651	UGUAUCC G CUGAUGAA	5755	TTCATCAG GGCTAGCTACAACGA GGGATACA	14504
5647	UCCCGCUG A UGAAAUUC	5756	GAATTTCA GGCTAGCTACAACGA CAGCGGGA	14505
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5637	GAAAUUCC A CAUGUGCU	5758	AGCACATG GGCTAGCTACAACGA GGAATTTT	14507
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5633	UUCCACAU G UGUUCGCG	5760	GCGAAGCA GGCTAGCTACAACGA ATGTGGAA	14509
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5617	CCCAGAAA G CCUCAAGG	5763	CCTTGAGG GGCTAGCTACAACGA TTTCTGGG	14512
5608	CCUCAAGG G CUCGCCAC	5764	GTGGCGAG GGCTAGCTACAACGA CCTTGAGG	14513
5604	AAGGGCUC G CCACUUGG	5765	CCAAGTGG GGCTAGCTACAACGA GAGCCCTT	14514
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5575	GAGCAGCA G CCUCCGCU	5772	AGCGGAGG GGCTAGCTACAACGA TGCTGCTC	14521
5569	CAGCCUCC G CUUGGUUG	5773	CAACCAAG GGCTAGCTACAACGA GGAGGCTG	14522
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5550	GGCUGUUU G GACAAUC	5778	GATTGCTG GGCTAGCTACAACGA AAACAGCC	14527
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5536	AUCCGAGC G CCUUCUGC	5782	GCAGAAGG GGCTAGCTACAACGA GCTCGGAT	14531
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5523	CUGCUUGA A CUGCUCGG	5784	CCGAGCAG GGCTAGCTACAACGA TCAAGCAG	14533
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5515	ACUGCUCG G CGAGCUGC	5786	GCAGCTCG GGCTAGCTACAACGA CGAGCAGT	14535
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5454	CUCAUCGA A CUCCUGGU	5800	ACCAGGAG GGCTAGCTACAACGA TCGATGAG	14549
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5415	AACAGCCG G CUUCCCGG	5807	CCGGGAAG GGCTAGCTACAACGA CGGCTGTT	14556
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5344	UCAGAGCU G CCAGGACG	5826	CGTCCTGG GGCTAGCTACAACGA AGCTCTGA	14575
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5336	GCCAGGAC G CCACCUAC	5828	GTAGGTGG GGCTAGCTACAACGA GTCCTGGC	14577
5333	AGGACGCC A CCUACUAG	5829	CTAGTAGG GGCTAGCTACAACGA GGCCTCCT	14578
5329	CGCCACCU A CUAGCACC	5830	GGTGCTAG GGCTAGCTACAACGA AGGTGGCG	14579
5325	ACCUACUA G CACCCAGG	5831	CCTGGGTG GGCTAGCTACAACGA TAGTAGGT	14580
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5315	ACCCAGGU G CUGGUGAC	5834	GTCACGAG GGCTAGCTACAACGA ACCTGGGT	14583
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5271	CAUGAUGU A UUUUGGUA	5848	TAACCAAA GGCTAGCTACAACGA ACATCATG	14597
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5256	UAUGGGGU G UGUGAGGG	5852	CCCTCACA GGCTAGCTACAACGA ACCCATA	14601
5254	UGGGGUGU G UGAGGGUG	5853	CACCCTCA GGCTAGCTACAACGA ACACCCCA	14602
5248	GUGUGAGG G UGACAUCA	5854	TGATGTCA GGCTAGCTACAACGA CCTCACAC	14603
5245	UGAGGGUG A CAUCAUUU	5855	AAATGATG GGCTAGCTACAACGA CACCCTCA	14604
5243	AGGGUGAC A UCAUUUUG	5856	CAAAATGA GGCTAGCTACAACGA GTCACCCT	14605
5240	GUGACAUC A UUUUGGAC	5857	GTCCAAAA GGCTAGCTACAACGA GATGTCAC	14606
5233	CAUUUUGG A CGGCUCCU	5858	AGGAGCCG GGCTAGCTACAACGA CCAAATG	14607
5230	UUUGGACG G CUCCUAGC	5859	GCTAGGAG GGCTAGCTACAACGA CGTCCAAA	14608
5223	GGCUCCUA G CCUAUACA	5860	TGTATAGG GGCTAGCTACAACGA TAGGAGCC	14609
5219	CCUAGCCU A UACAGCAG	5861	CTGCTGTA GGCTAGCTACAACGA AGGCTAGG	14610
5217	UAGCCUAU A CAGCAGGG	5862	CCCTGCTG GGCTAGCTACAACGA ATAGGCTA	14611
5214	CCUAUACA G CAGGGGUG	5863	CACCCCTG GGCTAGCTACAACGA TGTATAGG	14612
5208	CAGCAGGG G UGUUGGCC	5864	GGCCAACA GGCTAGCTACAACGA CCCTGCTG	14613
5206	GCAGGGGU G UUGGCCCC	5865	CGGGCCAA GGCTAGCTACAACGA ACCCCTGC	14614
5202	GGGUGUUG G CCCGUGUA	5866	TACACGGG GGCTAGCTACAACGA CAACACCC	14615
5198	GUUGGCCC G UGUAGCGU	5867	ACGTACA GGCTAGCTACAACGA GGGCCAAC	14616
5196	UGGCCCCG G UAGCGUAG	5868	CTACGCTA GGCTAGCTACAACGA TACGGCCA	14617
5193	CCCGUGUA G CGUAGGCU	5869	AGCCTACG GGCTAGCTACAACGA TACGCGG	14618
5191	CGUGUAGC G UAGGCUUU	5870	AAAGCCTA GGCTAGCTACAACGA GCTACACG	14619
5187	UAGCGUAG G CUUUAGCC	5871	GGCTAAAG GGCTAGCTACAACGA CTACGCTA	14620
5181	AGGCUUUA G CCGUGUGA	5872	TCACACGG GGCTAGCTACAACGA TAAAGCCT	14621
5178	CUUUAGCC G UGUGAGAC	5873	GTCTCACA GGCTAGCTACAACGA GGCTAAAG	14622

5176	UUAGCCGU G UGAGACAC	5874	GTGTCTCA GGCTAGCTACAACGA ACGGCTAA	14623
5171	CGUGUGAG A CACUCCA	5875	TGGAAGTG GGCTAGCTACAACGA CTCACACG	14624
5169	UGUGAGAC A CUUCCACA	5876	TGTGGAAG GGCTAGCTACAACGA GTCTCACA	14625
5163	ACACUCC A CAUUUGAU	5877	ATCAAATG GGCTAGCTACAACGA GGAAGTGT	14626
5161	ACUCCAC A UUUGAUCC	5878	GGATCAA GGCTAGCTACAACGA GTGGAAGT	14627
5156	CACAUUUG A UCCCACGA	5879	TCGTGGGA GGCTAGCTACAACGA CAAATGTG	14628
5151	UGAUCCC A CGAUGGGG	5880	CCCCATCG GGCTAGCTACAACGA GGGATCAA	14629
5148	AUCCCACG A UGGGGGUG	5881	CACCCCCA GGCTAGCTACAACGA CGTGGGAT	14630
5142	CGAUGGGG G UGGAGCCU	5882	AGGCTCCA GGCTAGCTACAACGA CCCCATCG	14631
5137	GGGGUGGA G CCUGAGCC	5883	GGCTCAGG GGCTAGCTACAACGA TCCACCCC	14632
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5125	GAGCCCUG G CGCACACU	5885	AGTGTGCG GGCTAGCTACAACGA CAGGGCTC	14634
5123	GGCCUGGC G CACACUGU	5886	ACAGTGTG GGCTAGCTACAACGA GCCAGGGC	14635
5121	CCUGGCGC A CACUGUGG	5887	CCACAGTG GGCTAGCTACAACGA GGCACAGG	14636
5119	UGGCGCAC A CUGUGGCU	5888	AGCCACAG GGCTAGCTACAACGA GTGCGCCA	14637
5116	CGCACACU G UGGCUUGG	5889	CCAAGCCA GGCTAGCTACAACGA AGTGTGCG	14638
5113	ACACUGUG G CUUGGUU	5890	ATACCAAG GGCTAGCTACAACGA CACAGTGT	14639
5108	GUGGCUUG G UAUGCAC	5891	GTAGCATA GGCTAGCTACAACGA CAAGCCAC	14640
5106	GGCUUGGU A UGCUACCA	5892	TGGTAGCA GGCTAGCTACAACGA ACCAAGCC	14641
5104	CUUGGUU G CUACCAGG	5893	CCTGGTAG GGCTAGCTACAACGA ATACCAAG	14642
5101	GGUAUGCU A CCAGGUAG	5894	CTACCTGG GGCTAGCTACAACGA AGCATACC	14643
5096	GUUACAG G UAGGGGAG	5895	CTCCCCTA GGCTAGCTACAACGA CTGGTAGC	14644
5087	UAGGGGAG G UUUUCUCC	5896	GGAGAAAA GGCTAGCTACAACGA CTCCCCTA	14645
5077	UUUCUCCU G CCUGCUUG	5897	CAAGCAGG GGCTAGCTACAACGA AGGAGAAA	14646
5073	UCCUGCCU G CUUGGUCU	5898	AGACCAAG GGCTAGCTACAACGA AGGCAGGA	14647
5068	CCUGCUUG G UCUGGGAC	5899	GTCCACGA GGCTAGCTACAACGA CAAGCAGG	14648
5061	GGUCUGGG A CAAGAAGU	5900	ACTTCTTG GGCTAGCTACAACGA CCCAGACC	14649
5054	GACAAGAA G UGGGCAUC	5901	GATGCCCA GGCTAGCTACAACGA TTCTTGTC	14650
5050	AGAAGUGG G CAUCUAUG	5902	CATAGATG GGCTAGCTACAACGA CCACTTCT	14651
5048	AAGUGGGC A UCUAUGUG	5903	CACATAGA GGCTAGCTACAACGA GCCCACTT	14652
5044	GGGCAUCU A UGUGGGUG	5904	CACCCACA GGCTAGCTACAACGA AGATGCCC	14653
5042	GCAUCUAU G UGGGUGAG	5905	CTCACCCA GGCTAGCTACAACGA ATAGATGC	14654
5038	CUAUGUGG G UGAGGCCU	5906	AGGCCTCA GGCTAGCTACAACGA CCACATAG	14655
5033	UGGGUGAG G CCUGUGAA	5907	TTCACAGA GGCTAGCTACAACGA CTCACCCA	14656
5029	UGAGGCCU G UGAAGACA	5908	TGTCTTCA GGCTAGCTACAACGA AGGCCCTA	14657
5023	CUGUGAAG A CACCCUCC	5909	GGAGGGTG GGCTAGCTACAACGA CTTACAG	14658
5021	GUGAAGAC A CCCUCCCA	5910	TGGGAGGG GGCTAGCTACAACGA GTCTTCAC	14659
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4983	GAAGGGCA A CCCUGGUG	5916	CACCAAGG GGCTAGCTACAACGA TGCCCTTC	14665
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4975	ACCCUGGU G UAUUUAGG	5918	CCTAAATA GGCTAGCTACAACGA ACCAGGGT	14667
4973	CCUGGUGU A UUUAGGUA	5919	TACCTAAA GGCTAGCTACAACGA ACACCAGG	14668
4967	GUUUUUAG G UAAGCCCG	5920	CGGGCTTA GGCTAGCTACAACGA CTAAATAC	14669
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4959	GUAAGCCC G CAACCUAA	5922	TTAGGTTG GGCTAGCTACAACGA GGGCTTAC	14671
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4951	GCAACCUA A CGAGGUC	5924	GACCTCCG GGCTAGCTACAACGA TAGGTTGC	14673
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4935	CUCGGCGG G CGUGAGCU	5927	AGCTCACG GGCTAGCTACAACGA CCGCCGAG	14676
4933	CGGCGGGC G UGAGCUCG	5928	CGAGCTCA GGCTAGCTACAACGA GCCCGCCG	14677
4929	GGGCGUGA G CUCGUACC	5929	GGTACGAG GGCTAGCTACAACGA TCACGCCC	14678

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4923	GAGCUCGU A CCAAGCAC	5931	GTGCTTGG GGCTAGCTACAACGA ACGAGCTC	14680
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4914	CCAAGCAC A UCCCGCGU	5934	ACGCGGGA GGCTAGCTACAACGA GTGCTTGG	14683
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4904	CCC CGCUC A UAGCACUC	5937	GAGTGCTA GGCTAGCTACAACGA GACGCGGG	14686
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4860	CGAAGGCC G CCUCUCUG	5948	CAGGAGAG GGCTAGCTACAACGA GGCCTTCG	14697
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4838	ACAAACCU G UAUAUGCC	5952	GGCATATA GGCTAGCTACAACGA AGGTTTGT	14701
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4509	G AUGAGAU G CCUCCCCC	6037	GGGGGAGG GGCTAGCTACAACGA ATCTCATC	14786
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4492	CUUUGAUG G UCUCGAUG	6039	CATCGAGA GGCTAGCTACAACGA CATCAAAG	14788
4486	UGGUCUCG A UGGGGAUG	6040	CATCCCCA GGCTAGCTACAACGA CGAGACCA	14789
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4443	GGUGUUGG A CAAGGCUA	6048	TAGCCTTG GGCTAGCTACAACGA CCAACACC	14797
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4435	ACAAGGCU A UCUCUCCG	6050	CGAGGAGA GGCTAGCTACAACGA AGCCTTGT	14799
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4424	UCCUCGAU G UUGGGAUG	6052	CATCCCAA GGCTAGCTACAACGA ATCGAGGA	14801
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4363	CGAGCCGC G CUCCAGCC	6070	GGCTGGAG GGCTAGCTACAACGA GCGGCTCG	14819
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4354	CUCCAGCC G UCUCGCU	6072	AGCGGAGA GGCTAGCTACAACGA GGCTGGAG	14821
4348	CCGUCUCC G CUUGGUCC	6073	GGACCAAG GGCTAGCTACAACGA GGAGACGG	14822
4343	UCCGCUUG G UCCAGGAC	6074	GTCTTGGA GGCTAGCTACAACGA CAAGCGGA	14823
4336	GGUCCAGG A CUGUGCCG	6075	CGGCACGA GGCTAGCTACAACGA CCTGGACC	14824
4333	CCAGGACU G UGCCGAUG	6076	CATCGGCA GGCTAGCTACAACGA AGTCTGTG	14825
4331	AGGACUGU G CCGAUGCC	6077	GGCATCGG GGCTAGCTACAACGA ACAGTCCT	14826
4327	CUGUGCCG A UGCCAAA	6078	TTTGGGCA GGCTAGCTACAACGA CGGCACAG	14827
4325	GUGCCGAU G CCAAAAU	6079	ATTTTGGG GGCTAGCTACAACGA ATCGGCAC	14828
4318	UGCCAAA A UGGAAGUC	6080	GACTTCCA GGCTAGCTACAACGA TTTGGGCA	14829
4312	AAAUGGAA G UCGAGUCA	6081	TGACTCGA GGCTAGCTACAACGA TTCCATTT	14830
4307	GAAGUCGA G UCAAUUGA	6082	TCAATTGA GGCTAGCTACAACGA TCGACTTC	14831
4303	UCGAGUCA A UUGAGUGG	6083	CCACTCAA GGCTAGCTACAACGA TGAATCGA	14832
4298	UCAAUUGA G UGGCACUC	6084	GAGTGCCA GGCTAGCTACAACGA TCAATTGA	14833
4295	AUUGAGUG G CACUCAUC	6085	GATGAGTG GGCTAGCTACAACGA CACTCAAT	14834
4293	UGAGUGGC A CUCAUCAC	6086	GTGATGAG GGCTAGCTACAACGA GCCACTCA	14835
4289	UGGCACUC A UCACACAU	6087	ATGTGTGA GGCTAGCTACAACGA GAGTGCCA	14836
4286	CACUCAUC A CACAUUAU	6088	ATAATGTG GGCTAGCTACAACGA GATGAGTG	14837
4284	CUCAUCAC A CAUUAUGA	6089	TCATAATG GGCTAGCTACAACGA GTGATGAG	14838
4282	CAUCACAC A UUAUGAUG	6090	CATCATAA GGCTAGCTACAACGA GTGTGATG	14839
4279	CACACAUU A UGAUGUCA	6091	TGACATCA GGCTAGCTACAACGA AATGTGTG	14840
4276	ACAUAUAG A UGUCAUAG	6092	CTATGACA GGCTAGCTACAACGA CATAATGT	14841
4274	AUAUAUAG G UCAUAGGC	6093	GCCTATGA GGCTAGCTACAACGA ATCATAAT	14842
4271	AUGAUGUC A UAGGCGCC	6094	GGCGCCTA GGCTAGCTACAACGA GACATCAT	14843
4267	UGUCAUAG G CGCCCCCA	6095	TGGGGGCG GGCTAGCTACAACGA CTATGACA	14844
4265	UCAUAGGC G CCCCCAGA	6096	TCTGGGGG GGCTAGCTACAACGA GCCTATGA	14845
4256	CCCCCAGA G CAACCACC	6097	GGTGGTTG GGCTAGCTACAACGA TCTGGGGG	14846

4253	CCAGAGCA A CCACCGUC	6098	GACGGTGG GGCTAGCTACAACGA TGCTCTGG	14847
4250	GAGCAACC A CCGUCGGC	6099	GCCGACGG GGCTAGCTACAACGA GGTGCTC	14848
4247	CAACCACC G UCGGCAAG	6100	CTTGCCGA GGCTAGCTACAACGA GGTGGTTG	14849
4243	CACCGUCG G CAAGGAAC	6101	GTTCTTGG GGCTAGCTACAACGA CGACGGTG	14850
4236	GGCAAGGA A CUUGCCAU	6102	ATGGCAAG GGCTAGCTACAACGA TCCTTGCC	14851
4232	AGGAACUU G CCAUAGGU	6103	ACCTATGG GGCTAGCTACAACGA AAGTTCCT	14852
4229	AACUUGCC A UAGGUGGA	6104	TCCACCTA GGCTAGCTACAACGA GGCAAGTT	14853
4225	UGCCAUAG G UGGAGUAC	6105	GTACTCCA GGCTAGCTACAACGA CTATGGCA	14854
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4218	GGUGGAGU A CGUGAUGG	6107	CCATCAGC GGCTAGCTACAACGA ACTCCACC	14856
4216	UGGAGUAC G UGAUGGGG	6108	CCCCACG GGCTAGCTACAACGA GTACTCCA	14857
4213	AGUACGUG A UGGGGGCG	6109	CGCCCCCA GGCTAGCTACAACGA CACGTACT	14858
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4205	AUGGGGGC G CCCGUGGU	6111	ACCACGGG GGCTAGCTACAACGA GCCCCCAT	14860
4201	GGGCGCCC G UGGUGAUG	6112	CATCACCA GGCTAGCTACAACGA GGGCGCCC	14861
4198	CGCCCGUG G UGAUGGUC	6113	GACCATCA GGCTAGCTACAACGA CACGGGCG	14862
4195	CCGUGGUG A UGGUCCUU	6114	AAGGACCA GGCTAGCTACAACGA CACCACGG	14863
4192	UGGUGAUG G UCCUUACC	6115	GGTAAGGA GGCTAGCTACAACGA CATCACCA	14864
4186	UGGUCCUU A CCCAGUU	6116	AACTGGGG GGCTAGCTACAACGA AAGGACCA	14865
4180	UUACCCCA G UUCUGAUG	6117	CATCAGAA GGCTAGCTACAACGA TGGGGTAA	14866
4174	CAGUUCUG A UGUUAGGA	6118	TCCTAACA GGCTAGCTACAACGA CAGAACTG	14867
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4166	AUGUUAGG A UCGACACC	6120	GGTGTGCA GGCTAGCTACAACGA CCTAACAT	14869
4162	UAGGAUCG A CACCGUGU	6121	ACACGGTG GGCTAGCTACAACGA CGATCCTA	14870
4160	GGAUCCGAC A CCGUGUGC	6122	GCACACGG GGCTAGCTACAACGA GTCGATCC	14871
4157	UCGACACC G UGUGCCUU	6123	AAGGCACA GGCTAGCTACAACGA GGTGTGCA	14872
4155	GACACCGU G UGCCUUAG	6124	CTAAGGCA GGCTAGCTACAACGA ACGGTGTC	14873
4153	CACCGUGU G CCUUAGAC	6125	GTCTAAGG GGCTAGCTACAACGA ACACGGTG	14874
4146	UGCCUUAG A CAUAUACG	6126	CGTATATG GGCTAGCTACAACGA CTAAGGCA	14875
4144	CCUUAGAC A UAUACGCC	6127	GGCGTATA GGCTAGCTACAACGA GTCTAAGG	14876
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4138	ACAUUAUC G CCCCAAAC	6130	GTTTGGGG GGCTAGCTACAACGA GTATATGT	14879
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4093	GGACGAGC A CUUUGUAC	6140	GTACAAAG GGCTAGCTACAACGA GCTCGTCC	14889
4088	AGCACUUU G UACCCUUG	6141	CAAGGGTA GGCTAGCTACAACGA AAAGTGCT	14890
4086	CACUUUGU A CCCUUGGG	6142	CCCAAGGG GGCTAGCTACAACGA ACAAAGTG	14891
4078	ACCCUUGG G CUGCAUUA	6143	ATATGCAG GGCTAGCTACAACGA CCAAGGGT	14892
4075	CUUGGGCU G CAUAUGCA	6144	TGCATATG GGCTAGCTACAACGA AGCCCAAG	14893
4073	UGGGCUGC A UAUGCAGC	6145	GCTGCATA GGCTAGCTACAACGA GCAGCCCA	14894
4071	GGCUGCAU A UGCAGCCG	6146	CGGCTGCA GGCTAGCTACAACGA ATGCAGCC	14895
4069	CUGCAUUA G CAGCCGGU	6147	ACCGGCTG GGCTAGCTACAACGA ATATGCAG	14896
4066	CAUAUGCA G CCGGUACC	6148	GGTACCGG GGCTAGCTACAACGA TGCATATG	14897
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4060	CAGCCGGU A CCUUAGUG	6150	CACTAAGG GGCTAGCTACAACGA ACCGGCTG	14899
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4052	ACCUUAGU G CUCUUGCC	6152	GGCAAGAG GGCTAGCTACAACGA ACTAAGGT	14901
4046	GUGCUCUU G CCGCUGCC	6153	GGCAGCGG GGCTAGCTACAACGA AAGAGCAC	14902

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4030	CAGUGGGA G CGUGUAGG	6157	CCTACACG GGCTAGCTACAACGA TCCCACTG	14906
4028	GUGGGAGC G UGUAGGUG	6158	CACCTACA GGCTAGCTACAACGA GCTCCAC	14907
4026	GGGAGCGU G UAGGUGGG	6159	CCCACCTA GGCTAGCTACAACGA ACGCTCCC	14908
4022	GCGUGUAG G UGGGCCAC	6160	GTGGCCCA GGCTAGCTACAACGA CTACACGC	14909
4018	GUAGGUGG G CCACUUGG	6161	CCAAGTGG GGCTAGCTACAACGA CCACCTAC	14910
4015	GGUGGGCC A CUUGGAAU	6162	ATTCCAAG GGCTAGCTACAACGA GGCCCACC	14911
4008	CACUUGGA A UGUCUGCG	6163	CGCAGACA GGCTAGCTACAACGA TCCAAGTG	14912
4006	CUUGGAAU G UCUGCGGU	6164	ACCGCAGA GGCTAGCTACAACGA ATTCCAAG	14913
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3984	UGGGGGGG A CGAGUUGU	6169	ACAACCTG GGCTAGCTACAACGA CCCCCCA	14918
3980	GGGGACGA G UUGUCCGU	6170	ACGGACAA GGCTAGCTACAACGA TCGTCCCC	14919
3977	GACGAGUU G UCCGUGAA	6171	TTCACCTA GGCTAGCTACAACGA AACTCGTC	14920
3973	AGUUGUCC G UGAAGACC	6172	GGTCTTGA GGCTAGCTACAACGA GGACAAC	14921
3967	CCGUGAAG A CCGGGGAC	6173	GTCCCCGG GGCTAGCTACAACGA CTTACCGG	14922
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3957	CGGGGACC G CAUGGUAG	6175	CTACCATG GGCTAGCTACAACGA GGTCCCCG	14924
3955	GGGACCGC A UGGUAGUU	6176	AACTACCA GGCTAGCTACAACGA GCGGTCCC	14925
3952	ACCGCAUG G UAGUUUCC	6177	GGAAACTA GGCTAGCTACAACGA CATGCGGT	14926
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3939	UUCCAUGA A CUCAACGG	6180	CCGTTGAG GGCTAGCTACAACGA CTATGGAA	14929
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3923	GGUACAAA G UCCACCGC	6184	GCGGTGGA GGCTAGCTACAACGA TTTGTACC	14933
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3916	AGUCCACC G CCUUCGCA	6186	TGCGAAGG GGCTAGCTACAACGA GGTGGACT	14935
3910	CCGCCUUC G CAACCCCC	6187	GGGGGTTG GGCTAGCTACAACGA GAAGGCGG	14936
3907	CCUUCGCA A CCCCCCGG	6188	CCGGGGGG GGCTAGCTACAACGA TGCGAAGG	14937
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3814	AGUAGGAG A UGGGCCUG	6208	CAGGCCCA GGCTAGCTACAACGA CTCCTACT	14957
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3785	CUCCCCCU G CUGUCACC	6213	GGTGACAG GGCTAGCTACAACGA AGGGGGAG	14962
3782	CCCCUGCU G UCACCCCG	6214	CGGGGTGA GGCTAGCTACAACGA AGCAGGGG	14963
3779	CUGCUGUC A CCCC GCCG	6215	CGGCGGGG GGCTAGCTACAACGA GACAGCAG	14964
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3667	GCCAUCGG A CGAGGUCC	6245	GGACCTCG GGCTAGCTACAACGA CGGATGGC	14994
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3575	ACAGUCCA G CACACGCC	6267	GGCGTGTG GGCTAGCTACAACGA TGGACTGT	15016
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3566	CACACGCC G UUGACGCA	6271	TGCGTCAA GGCTAGCTACAACGA GGCCTGTG	15020
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3560	CCGUUGAC G CAGGUCGC	6273	GCGACCTG GGCTAGCTACAACGA GTCAACGG	15022
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3553	CGCAGGUC G CUAGGAAA	6275	TTTCCTAG GGCTAGCTACAACGA GACCTGCG	15024
3543	UAGGAAAG A CUGCGUCG	6276	CGACGCAG GGCTAGCTACAACGA CTTTCCTA	15025
3540	GAAAGACU G CGUCGCGG	6277	CCGCGACG GGCTAGCTACAACGA AGTCTTTC	15026
3538	AAGACUGC G UCGCGGUG	6278	CACCGCGA GGCTAGCTACAACGA GCAGTCTT	15027
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3532	GCGUCGCG G UGGAAACC	6280	GGTTTCCA GGCTAGCTACAACGA CGCGACGC	15029
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3523	UGGAAACC A CUUGAACU	6282	AGTTCAAG GGCTAGCTACAACGA GGTTCCTA	15031
3517	CCACUUGA A CUUCCCC	6283	GGGGGAAG GGCTAGCTACAACGA TCAAGTGG	15032
3505	CCCCCUCG A CUUGGUUC	6284	GAAACCAAG GGCTAGCTACAACGA CGAGGGGG	15033
3500	UCGACUUG G UUCUUGUC	6285	GACAAGAA GGCTAGCTACAACGA CAAGTCGA	15034
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3479	CCCGUGAG G CUGGUGAU	6289	ATCACCAG GGCTAGCTACAACGA CTCACGGG	15038
3475	UGAGGCUG G UGAUAAUG	6290	CATTATCA GGCTAGCTACAACGA CAGCCTCA	15039
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3459	GCAGCCAA A CAGGCCCC	6295	GGGGCCTG GGCTAGCTACAACGA TTGGCTGC	15044
3455	CCAAACAG G CCCCAGCU	6296	ACGCGGGG GGCTAGCTACAACGA CTGTTTGG	15045
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3448	GGCCCCGC G UCUGUUGG	6298	CCAACAGA GGCTAGCTACAACGA GCGGGGCC	15047
3444	CCGCGUCU G UUGGGAGU	6299	ACTCCCAA GGCTAGCTACAACGA AGACGCGG	15048
3437	UGUUGGGA G UAGGCCGU	6300	ACGGCCTA GGCTAGCTACAACGA TCCCAACA	15049
3433	GGGAGUAG G CCGUAAUG	6301	CATTACGA GGCTAGCTACAACGA TGACTCCC	15050
3430	AGUAGGCC G UAAUGGGC	6302	GCCCATTA GGCTAGCTACAACGA GGCTTACT	15051
3427	AGGCCGUA A UGGGCGCG	6303	CGCGCCCA GGCTAGCTACAACGA TACGGCCT	15052
3423	CGUAAUGG G CGCGAGGA	6304	TCCTCGCG GGCTAGCTACAACGA CCATTACG	15053
3421	UAAUGGGC G CGAGGAGU	6305	ACTCCTCG GGCTAGCTACAACGA GCCCATTA	15054
3414	CGCGAGGA G UCGCCACC	6306	GGTGCGCA GGCTAGCTACAACGA TCCTCGCG	15055
3411	GAGGAGUC G CCACCCCU	6307	AGGGGTGG GGCTAGCTACAACGA GACTCCTC	15056
3408	GAGUCGCC A CCCCUGCC	6308	GGCAGGGG GGCTAGCTACAACGA GGCAGACT	15057
3402	CCACCCCU G CCCCUCAA	6309	TTGAGGGG GGCTAGCTACAACGA AGGGGTGG	15058
3392	CCCUCAAG A CUGUCGGC	6310	GCCGACAG GGCTAGCTACAACGA CTTGAGGG	15059
3389	UCAAGACU G UCGGCUGG	6311	CCAGCCGA GGCTAGCTACAACGA AGTCTTGA	15060
3385	GACUGUCG G CUGGUCCU	6312	AGGACCAG GGCTAGCTACAACGA CGACAGTC	15061
3381	GUCGGCUG G UCCUAGGA	6313	TCCTAGGA GGCTAGCTACAACGA CAGCCGAC	15062
3372	UCCUAGGA G UAUCUCCC	6314	GGGAGATA GGCTAGCTACAACGA TCCTAGGA	15063
3370	CUAGGAGU A UCUCUCCU	6315	GAGGGAGA GGCTAGCTACAACGA ACTCCTAG	15064
3352	CCCUUCGG G CGGAGACA	6316	TGTCTCCG GGCTAGCTACAACGA CCGAAGGG	15065
3346	GGGCGGAG A CAGGUAGA	6317	TCTACCTG GGCTAGCTACAACGA CTCGCCCC	15066
3342	GGAGACAG G UAGACCCA	6318	TGGGTCTA GGCTAGCTACAACGA CTGTCTCC	15067
3338	ACAGGUAG A CCCAUAAU	6319	ATTATGGG GGCTAGCTACAACGA CTACCTGT	15068
3334	GUAGACCC A UAAUGAUG	6320	CATCATTA GGCTAGCTACAACGA GGGTCTAC	15069
3331	GACCCAU A UGAUGUCC	6321	GGACATCA GGCTAGCTACAACGA TATGGGTC	15070

3328	CCAUAAUG A UGUCCCCA	6322	TGGGGACA GGCTAGCTACAACGA CATTATGG	15071
3326	AUAAUGAU G UCCCCACA	6323	TGTGGGGA GGCTAGCTACAACGA ATCATTAT	15072
3320	AUGUCCCC A CACGCCGC	6324	GCGGCGTG GGCTAGCTACAACGA GGGGACAT	15073
3318	GUCCCCAC A CGCCGCGG	6325	CCGCGGCG GGCTAGCTACAACGA GTGGGGAC	15074
3316	CCCCACAC G CCGCGGUG	6326	CACCGCGG GGCTAGCTACAACGA GTGTGGGG	15075
3313	CACACGCC G CGGUGUCU	6327	AGACACCG GGCTAGCTACAACGA GGCCTGTG	15076
3310	ACGCCGCG G UGUUCCCC	6328	GGGAGACA GGCTAGCTACAACGA CGCGCGCT	15077
3308	GCGCGGGU G UGUUCCCC	6329	GGGGGAGA GGCTAGCTACAACGA ACCGCGGC	15078
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3277	UGAUUUCU A UGUCCGAG	6334	CTCCGACA GGCTAGCTACAACGA GGAAATCA	15083
3275	AUUUCCAUG G UCGGAGAA	6335	TTCTCCGA GGCTAGCTACAACGA ATGGAAAT	15084
3265	CGGAGAAG A CGACGGGC	6336	GCCCGTCG GGCTAGCTACAACGA CTTCTCCG	15085
3262	AGAAGACG A CGGGCUCG	6337	CGAGCCCG GGCTAGCTACAACGA CGTCTTCT	15086
3258	GACGACGG G CUCGACCG	6338	CGGTCCGAG GGCTAGCTACAACGA CCGTCGTC	15087
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3244	CCGCUACC G CCAGGUCU	6342	AGACCTGG GGCTAGCTACAACGA GGTAGCGG	15091
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3230	UCUCGUAG A CCUGUGUG	6345	CACACAGG GGCTAGCTACAACGA CTACGAGA	15094
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3148	UGAAGGCC A UUUGGACA	6365	TGTCCAAA GGCTAGCTACAACGA GGCCTTCA	15114
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3109	GACCAAAA A UGCAUUCA	6374	TGAATGCA GGCTAGCTACAACGA TTTGGTGC	15123
3107	ACCAAAAU G CAUUCACG	6375	CGTGAATG GGCTAGCTACAACGA ATTTTGGT	15124
3105	CAAAAUGC A UUCACGGA	6376	TCCGTGAA GGCTAGCTACAACGA GCATTTTG	15125
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3085	CCCCUUGA G CCCGCACA	6380	TGTGCGGG GGCTAGCTACAACGA TCAAGGGG	15129
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3079	GAGCCCGC A CAAAGUCC	6382	GGACTTTG GGCTAGCTACAACGA GCGGGCTC	15131
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3069	AAAGUCCG G CACUUUUG	6384	CAAAAGTG GGCTAGCTACAACGA CGGACTTT	15133
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3056	UUUGCUAU A CCAGCCUG	6388	CAGGCTGG GGCTAGCTACAACGA ATAGCAAA	15137
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3045	AGCCUGGA G CACCAUGA	6390	TCATGGTG GGCTAGCTACAACGA TCCAGGCT	15139
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3040	GGAGCACC A UGAGCGGG	6392	CCCCTCA GGCTAGCTACAACGA GGTGCTCC	15141
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3027	CGGGCCGA G UAUGGCGA	6395	TCGCCATA GGCTAGCTACAACGA TCGGGCCG	15144
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3022	CGAGUAUG G CGAGCAUA	6397	TATGCTCG GGCTAGCTACAACGA CATACTCG	15146
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3013	CGAGCAUA A UUUGGUG	6400	CACCAAAA GGCTAGCTACAACGA TATGCTCG	15149
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2956	GAAUGAUG G CACCGCGC	6414	GCGCGGTG GGCTAGCTACAACGA CATCATTC	15163
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2936	CCCCGAAC G UUGAGGGG	6419	CCCCTCAA GGCTAGCTACAACGA GTTCGGGG	15168
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2917	GGAUCCAC A CUUGCAAC	6422	GTTGCAAG GGCTAGCTACAACGA GTGGATCC	15171
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2547	CAUCAUCC A CAAACAGG	6518	CCTGTTTG GGCTAGCTACAACGA GGATGATG	15267
2543	AUCCACAA A CAGGCACA	6519	TGTGCCTG GGCTAGCTACAACGA TTGTGGAT	15268
2539	ACAAACAG G CACAGACG	6520	CGTCTGTG GGCTAGCTACAACGA CTGTTTGT	15269
2537	AAACAGGC A CAGACGCG	6521	CGCGTCTG GGCTAGCTACAACGA GCCTGTTT	15270
2533	AGGCACAG A CGCGCGCG	6522	CGCGCGCG GGCTAGCTACAACGA CTGTGCCT	15271
2531	GCACAGAC G CGCGCGUC	6523	GACGCGCG GGCTAGCTACAACGA GTCTGTGC	15272
2529	ACAGACGC G CGCGUCUG	6524	CAGACGCG GGCTAGCTACAACGA GCGTCTGT	15273
2527	AGACGCGC G CGUCUGCC	6525	GGCAGCGG GGCTAGCTACAACGA GCGCGTCT	15274
2525	ACGCGCGC G UCUGCCAG	6526	CTGGCAGA GGCTAGCTACAACGA GCGCGCGT	15275
2521	GCGCGUCU G CCAGGAGA	6527	TCTCCTGG GGCTAGCTACAACGA AGACGCGC	15276
2505	AAGGAAAA G CAACAGGA	6528	TCCTGTTG GGCTAGCTACAACGA TTTTCCTT	15277
2502	GAAAAGCA A CAGGACAU	6529	ATGTCCTG GGCTAGCTACAACGA TGCTTTTC	15278
2497	GCAACAGG A CAUACUCC	6530	GGAGTATG GGCTAGCTACAACGA CCTGTTGC	15279
2495	AACAGGAC A UACUCCCA	6531	TGGGAGTA GGCTAGCTACAACGA GTCCTGTT	15280
2493	CAGGACAU A CUCCCAU	6532	AATGGGAG GGCTAGCTACAACGA ATGTCCTG	15281
2487	AUACUCCC A UUUGAUUG	6533	CAATCAAA GGCTAGCTACAACGA GGGAGTAT	15282
2482	CCCAUUUG A UUGCGAAG	6534	CTTCGCAA GGCTAGCTACAACGA CAAATGGG	15283
2479	AUUUGAUU G CGAAGGAG	6535	CTCCTTCG GGCTAGCTACAACGA AATCAAAAT	15284
2470	CGAAGGAG A CAACCGCU	6536	AGCGGTTG GGCTAGCTACAACGA CTCCTTCG	15285
2467	AGGAGACA A CCGCUGAC	6537	GTCAGCGG GGCTAGCTACAACGA TGTCTCCT	15286
2464	AGACAACC G CUGACCCU	6538	AGGGTCAG GGCTAGCTACAACGA GGTGTGCT	15287
2460	AACCGCUG A CCCUACAC	6539	GTGTAGGG GGCTAGCTACAACGA CAGCGGTT	15288
2455	CUGACCCU A CACCGUAC	6540	GTACGGTG GGCTAGCTACAACGA AGGGTCAG	15289
2453	GACCCUAC A CCGUACAG	6541	CTGTACGG GGCTAGCTACAACGA GTAGGGTC	15290
2450	CCUACACC G UACAGGUA	6542	TACCTGTA GGCTAGCTACAACGA GGTGTAGG	15291
2448	UACACCGU A CAGGUAU	6543	AATACCTG GGCTAGCTACAACGA ACGGTGTA	15292
2444	CCGUACAG G UAUUGCAC	6544	GTGCAATA GGCTAGCTACAACGA CTGTACGG	15293
2442	GUACAGGU A UUGCACGU	6545	ACGTGCAA GGCTAGCTACAACGA ACCTGTAC	15294

2439	CAGGUAUU G CACGUCCA	6546	TGGACGTG GGCTAGCTACAACGA AATACCTG	15295
2437	GGUAUUGC A CGUCCACG	6547	CGTGGACG GGCTAGCTACAACGA GCAATACC	15296
2435	UAUUGCAC G UCCACGAU	6548	ATCGTGGA GGCTAGCTACAACGA GTGCAATA	15297
2431	GCACGUCC A CGAUGUUC	6549	GAACATCG GGCTAGCTACAACGA GGACGTGC	15298
2428	CGUCCACG A UGUUCUGG	6550	CCAGAACA GGCTAGCTACAACGA CGTGGACG	15299
2426	UCCACGAU G UUCUGGUG	6551	CACCAGAA GGCTAGCTACAACGA ATCGTGGA	15300
2420	AUGUUCUG G UGGAGAUG	6552	CATCTCCA GGCTAGCTACAACGA CAGAACAT	15301
2414	UGGUGGAG A UGGAUCAA	6553	TTGATCCA GGCTAGCTACAACGA CTCCACCA	15302
2410	GGAGAUGG A UCAAACCA	6554	TGGTTTGA GGCTAGCTACAACGA CCATCTCC	15303
2405	UGGAUCAA A CCAGUGGA	6555	TCCACTGG GGCTAGCTACAACGA TTGATCCA	15304
2401	UCAAACCA G UGGACAGA	6556	TCTGTCCA GGCTAGCTACAACGA TGGTTTGA	15305
2397	ACCAGUGG A CAGAGCCG	6557	CGGCTCTG GGCTAGCTACAACGA CCACTGGT	15306
2392	UGGACAGA G CCGGUAGG	6558	CCTACCGG GGCTAGCTACAACGA TCTGTCCA	15307
2388	CAGAGCCG G UAGGGUGG	6559	CCACCCTA GGCTAGCTACAACGA CGGCTCTG	15308
2383	CCGGUAGG G UGGUGAAG	6560	CTTCACCA GGCTAGCTACAACGA CCTACCGG	15309
2380	GUAGGGUG G UGAAGGAG	6561	CTCCTTCA GGCTAGCTACAACGA CACCCTAC	15310
2372	GUGAAGGA G CAGGGCAG	6562	CTGCCCTG GGCTAGCTACAACGA TCCTTCAC	15311
2367	GGAGCAGG G CAGUAUUU	6563	AAATACTG GGCTAGCTACAACGA CCTGTCTC	15312
2364	GACGGGCA G UAUUUGCC	6564	GGCAAATA GGCTAGCTACAACGA TGCCCTGC	15313
2362	AGGGCAGU A UUUGCCAC	6565	GTGGCAAA GGCTAGCTACAACGA ACTGCCCT	15314
2358	CAGUAUUU G CCACUCUG	6566	CAGAGTGG GGCTAGCTACAACGA AAATACTG	15315
2355	UAUUUGCC A CUCUGUAG	6567	CTACAGAG GGCTAGCTACAACGA GGCAAATA	15316
2350	GCCACUCU G UAGUGGAC	6568	GTCCACTA GGCTAGCTACAACGA AGAGTGGC	15317
2347	ACUCUGUA G UGGACAAC	6569	GTTGTCCA GGCTAGCTACAACGA TACAGAGT	15318
2343	UGUAGUGG A CAACAGCA	6570	TGCTGTTG GGCTAGCTACAACGA CCACTACA	15319
2340	AGUGGACA A CAGCAGCG	6571	CGCTGCTG GGCTAGCTACAACGA TGTCCACT	15320
2337	GGACAACA G CAGCGGGC	6572	GCCCGCTG GGCTAGCTACAACGA TGTGTGTC	15321
2334	CAACAGCA G CGGGCUGA	6573	TCAGCCCG GGCTAGCTACAACGA TGTGTGTTG	15322
2330	AGCAGCGG G CUGAGCUC	6574	GAGCTCAG GGCTAGCTACAACGA CCGCTGCT	15323
2325	CGGGCUGA G CUCUGAUC	6575	GATCAGAG GGCTAGCTACAACGA TCAGCCCG	15324
2319	GAGCUCUG A UCUGUCCC	6576	GGGACAGA GGCTAGCTACAACGA CAGAGCTC	15325
2315	UCUGAUCU G UCCCUGUC	6577	GACAGGGA GGCTAGCTACAACGA AGATCAGA	15326
2309	CUGUCCCU G UCCUCCAA	6578	TTGGAGGA GGCTAGCTACAACGA AGGGACAG	15327
2300	UCCUCCAA A UCACAACG	6579	CGTTGTGA GGCTAGCTACAACGA TTGGAGGA	15328
2297	UCCAAAUC A CAACGCUC	6580	GAGCGTTG GGCTAGCTACAACGA GATTGTGA	15329
2294	AAACACA A CGCUCUCC	6581	GGAGAGCG GGCTAGCTACAACGA GTGTGATT	15330
2292	AUCACAAC G CUCUCCUC	6582	GAGGAGAG GGCTAGCTACAACGA GTTGTGAT	15331
2281	CUCUCUGA G UCCAAUUG	6583	CAATTGGA GGCTAGCTACAACGA TCGAGGAG	15332
2276	CGAGUCCA A UUGCAUGC	6584	GCATGCAA GGCTAGCTACAACGA TGGACTCG	15333
2273	GUCCAAUU G CAUGC GGC	6585	GCCGCATG GGCTAGCTACAACGA AATTGGAC	15334
2271	CCAAUUGC A UGCGGCGG	6586	CCGCCGCA GGCTAGCTACAACGA GCAATTGG	15335
2269	AAUUGCAU G CGGCGGUG	6587	CACCGCCG GGCTAGCTACAACGA ATGCAATT	15336
2266	UGCAUGCG G CGGUGAGC	6588	GCTCACCG GGCTAGCTACAACGA CGCATGCA	15337
2263	AUGCGGCG G UGAGCCUG	6589	CAGGCTCA GGCTAGCTACAACGA CGCCGCAT	15338
2259	GGCGGUGA G CCUGUGCU	6590	AGCACAGG GGCTAGCTACAACGA TCACCGCC	15339
2255	GUGAGCCU G UGCUCCAC	6591	GTGGAGCA GGCTAGCTACAACGA AGGCTCAC	15340
2253	GAGCCUGU G CUCCACGC	6592	GCGTGGAG GGCTAGCTACAACGA ACAGGCTC	15341
2248	UGUGCUCC A CGCCCCC	6593	GGGGGGCG GGCTAGCTACAACGA GGAGCACA	15342
2246	UGCUCAC G CCCCCAC	6594	GTGGGGGG GGCTAGCTACAACGA GTGGAGCA	15343
2239	CGCCCCC A CAUACAUC	6595	GATGTATG GGCTAGCTACAACGA GGGGGGCG	15344
2237	CCCCCAC A UACAUCU	6596	AGGATGTA GGCTAGCTACAACGA GTGGGGGG	15345
2235	CCCCACAU A CAUCCUAA	6597	TTAGTAGT GGCTAGCTACAACGA ATGTGGGG	15346
2233	CCACAUAC A UCCUAAAC	6598	GTTTAGGA GGCTAGCTACAACGA GTATGTGG	15347
2227	ACAUCCUA A CCUUAAG	6599	CTTTAAGG GGCTAGCTACAACGA TAGGATGT	15348
2218	CCUUAAG A UGGAAAAA	6600	TTTTTCCA GGCTAGCTACAACGA CTTTAAGG	15349
2210	AUGGAAAA A UUGACAGU	6601	ACTGTCAA GGCTAGCTACAACGA TTTTCAT	15350

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2203	AAUUGACA G UGCAGGGG	6603	CCCCTGCA GGCTAGCTACAACGA TGTCATT	15352
2201	UUGACAGU G CAGGGGUA	6604	TACCCCTG GGCTAGCTACAACGA ACTGTCAA	15353
2195	GUGCAGGG G UAGUGCCA	6605	TGGCACTA GGCTAGCTACAACGA CCCTGCAC	15354
2192	CAGGGGUA G UGCCAAAG	6606	CTTTGGCA GGCTAGCTACAACGA TACCCCTG	15355
2190	GGGGUAGU G CCAAAGCC	6607	GGCTTTGG GGCTAGCTACAACGA ACTACCCC	15356
2184	GUGCCAAA G CCUGUAUG	6608	CATACAGG GGCTAGCTACAACGA TTTGGCAC	15357
2180	CAAAGCCU G UAUGGGUA	6609	TACCCATA GGCTAGCTACAACGA AGGCTTTG	15358
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2171	UAUGGGUA G UCAACUAU	6612	GTGTGTA GGCTAGCTACAACGA TACCCATA	15361
2167	GGUAGUCA A CUAUGCAU	6613	ATGCATGA GGCTAGCTACAACGA TGACTACC	15362
2164	AGUCAACU A UGCAUCUA	6614	TAGATGCA GGCTAGCTACAACGA AGTTGACT	15363
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2160	AACUAUGC A UCUAGGUG	6616	CACCTAGA GGCTAGCTACAACGA GCATAGTT	15365
2154	GCAUCUAG G UGUUAACC	6617	GGTTAACA GGCTAGCTACAACGA CTAGATGC	15366
2152	AUCUAGGU G UUAACCAA	6618	TTGGTTAA GGCTAGCTACAACGA ACCTAGAT	15367
2148	AGGUGUUA A CCAAGGCC	6619	GGCCTTGG GGCTAGCTACAACGA TAACACCT	15368
2142	UAACCAAG G CCCGAAC	6620	GTTCTGGG GGCTAGCTACAACGA CTTGGTTA	15369
2135	GGCCCCGA A CCGCACUU	6621	AAGTCGGG GGCTAGCTACAACGA TCGGGGCC	15370
2132	CCCGAACC G CACUUUGC	6622	GCAAAGTG GGCTAGCTACAACGA GGTTCGGG	15371
2130	CGAACCGC A CUUUGCGU	6623	ACGCAAAG GGCTAGCTACAACGA GCGGTTCTG	15372
2125	CGCACUUU G CGUAAGUG	6624	CACTTACG GGCTAGCTACAACGA AAAGTGG	15373
2123	CACUUUGC G UAAGUGGC	6625	GCCACTTA GGCTAGCTACAACGA GCAAAGTG	15374
2119	UUGCGUAA G UGGCCUCG	6626	CGAGGCCA GGCTAGCTACAACGA TTACGCAA	15375
2116	CGUAAGUG G CCUCGGGG	6627	CCCCGAGG GGCTAGCTACAACGA CACTTACG	15376
2108	GCCUCGGG G UGCUUCCG	6628	CGGAAGCA GGCTAGCTACAACGA CCCGAGGC	15377
2106	CUCGGGGU G CUUCCGGA	6629	TCCGGAAG GGCTAGCTACAACGA ACCCGAG	15378
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2093	CGGAAGCA G UCCGUGGG	6631	CCCACGGA GGCTAGCTACAACGA TGCTTCCG	15380
2089	AGCAGUCC G UGGGGCAG	6632	CTGCCCCA GGCTAGCTACAACGA GGACTGCT	15381
2084	UCCGUGGG G CAGGUUAA	6633	TTAACCTG GGCTAGCTACAACGA CCCACGGA	15382
2080	UGGGGCAG G UUAAGGUG	6634	CACCTTAA GGCTAGCTACAACGA CTGCCCCA	15383
2074	AGGUUAAG G UGUCGUUA	6635	TAACGACA GGCTAGCTACAACGA CTTAACCT	15384
2072	GUUAAGGU G UCGUUACC	6636	GGTAACGA GGCTAGCTACAACGA ACCTTAAC	15385
2069	AAGGUGUC G UAACCGGC	6637	GCCGGTAA GGCTAGCTACAACGA GACACCTT	15386
2066	GUGUCGUU A CCGCCCC	6638	GGGGCCGG GGCTAGCTACAACGA AACGACAC	15387
2062	CGUUACCG G CCCCCCG	6639	CGGGGGGG GGCTAGCTACAACGA CGGTAACG	15388
2053	CCCCCCCC G UGUUGCAC	6640	GTGCAACA GGCTAGCTACAACGA CGGGGGGG	15389
2051	CCCCCGAU G UUGCACGG	6641	CCGTGCAA GGCTAGCTACAACGA ATCGGGGG	15390
2048	CCGAUGUU G CACGGGGG	6642	CCCCCGTG GGCTAGCTACAACGA AACATCGG	15391
2046	GAUGUUGC A CGGGGGGC	6643	GCCCCCGG GGCTAGCTACAACGA GCAACATC	15392
2039	CACGGGGG G CCCCCGCA	6644	TGCGGGGG GGCTAGCTACAACGA CCCCCGTG	15393
2033	GGGCCCCC G CACGUCUU	6645	AAGACGTG GGCTAGCTACAACGA GGGGGCCC	15394
2031	GCCCCCGC A CGUCUUGG	6646	CCAAGACG GGCTAGCTACAACGA GCGGGGGC	15395
2029	CCCCGCAC G UCUUGGUG	6647	CACCAAGA GGCTAGCTACAACGA GTGCGGGG	15396
2023	ACGUCUUG G UGAACCCA	6648	TGGGTTCA GGCTAGCTACAACGA CAAGACGT	15397
2019	CUUGGUGA A CCCAGUGC	6649	GCACTGGG GGCTAGCTACAACGA TCACCAAG	15398
2014	UGAACCCA G UGCCAUUC	6650	GAATGGCA GGCTAGCTACAACGA TGGGTTCA	15399
2012	AACCCAGU G CCAUUCAU	6651	ATGAATGG GGCTAGCTACAACGA ACTGGGTT	15400
2009	CCAGUGCC A UUCAUCCA	6652	TGGATGAA GGCTAGCTACAACGA GGCACCTG	15401
2005	UGCCAUUC A UCCAUGUG	6653	CACATGGA GGCTAGCTACAACGA GAATGGCA	15402
2001	AUUCAUCC A UUGCAGC	6654	GCTGCACA GGCTAGCTACAACGA GGATGAAT	15403
1999	UCAUCCAU G UGCAGCCG	6655	CGGCTGCA GGCTAGCTACAACGA ATGGATGA	15404
1997	AUCCAUGU G CAGCCGAA	6656	TTGGGCTG GGCTAGCTACAACGA ACATGGAT	15405
1994	CAUGUGCA G CCGAACCA	6657	TGGTTCGG GGCTAGCTACAACGA TGCACATG	15406

1989	GCAGCCGA A CCAGUUGC	6658	GCAACTGG GGCTAGCTACAACGA TCGGCTGC	15407
1985	CCGAACCA G UUGCCUUG	6659	CAAGGCAA GGCTAGCTACAACGA TGGTTCGG	15408
1982	AACCAGUU G CCUUGCGG	6660	CCGCAAGG GGCTAGCTACAACGA AACTGGTT	15409
1977	GUUGCCUU G CGGCGGCC	6661	GGCCGCCG GGCTAGCTACAACGA AAGGCAAC	15410
1974	GCCUUGCG G CGGCCGCG	6662	CGCGGCCG GGCTAGCTACAACGA CGCAAGGC	15411
1971	UUGCGGCG G CCGCGUGU	6663	ACACGCGG GGCTAGCTACAACGA CGCCGCAA	15412
1968	CGCGGCC G CGUGUUGU	6664	ACAACACG GGCTAGCTACAACGA GGCCGCCG	15413
1966	GCGGCCCG G UGUUGUUG	6665	CAACAACA GGCTAGCTACAACGA GCGGCCGC	15414
1964	GGCCGCGU G UUGUUGAG	6666	CTCAACAA GGCTAGCTACAACGA ACGCGGCC	15415
1961	CGCGUGUU G UUGAGGAG	6667	CTCTCAA GGCTAGCTACAACGA AACACGCG	15416
1953	GUUGAGGA G CAGCACGU	6668	ACGTGCTG GGCTAGCTACAACGA TCCTCAAC	15417
1950	GAGGAGCA G CAGUCCG	6669	CGGACGTG GGCTAGCTACAACGA TGCTCCTC	15418
1948	GGAGCAGC A CGUCCGUC	6670	GACGGACG GGCTAGCTACAACGA GCTGCTCC	15419
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1942	GCACGUCC G UCUCGUUC	6672	GAACGAGA GGCTAGCTACAACGA GGACGTGC	15421
1937	UCCGUCUC G UUCGCCCC	6673	GGGGCGAA GGCTAGCTACAACGA GAGACGGA	15422
1933	UCUCGUUC G CCCCCAG	6674	CTGGGGGG GGCTAGCTACAACGA GAACGAGA	15423
1925	GCCCCCA G UUAUACGU	6675	ACGTATAA GGCTAGCTACAACGA TGGGGGGC	15424
1922	CCCCAGUU A UACGUGGG	6676	CCACGTA GGCTAGCTACAACGA AAGTGGGG	15425
1920	CCAGUUAU A CGUGGGGG	6677	CCCCCACG GGCTAGCTACAACGA ATAACTGG	15426
1918	AGUUAUAC G UGGGGGCG	6678	CGCCCCCA GGCTAGCTACAACGA GTATAACT	15427
1912	ACGUGGGG G CGCCGAAA	6679	TTTCGGCG GGCTAGCTACAACGA CCCCACGT	15428
1910	GUGGGGGC G CCGAAACG	6680	CGTTTCGG GGCTAGCTACAACGA GCCCCAC	15429
1904	GCGCCGAA A CGGUCGGU	6681	ACCGACCG GGCTAGCTACAACGA TTCGGCGC	15430
1901	CCGAAACG G UCGGUCGU	6682	ACGACCGA GGCTAGCTACAACGA CGTTTCGG	15431
1897	AACGGUCG G UCGUCCCC	6683	GGGGCGGA GGCTAGCTACAACGA CGACCGTT	15432
1894	GGUCGGUC G UCCCCACC	6684	GGTGGGGA GGCTAGCTACAACGA GACCGACC	15433
1888	UCGUCCCC A CCACAACA	6685	TGTTGTGG GGCTAGCTACAACGA GGGGACGA	15434
1885	UCCCCACC A CAACAGGG	6686	CCCTGTTG GGCTAGCTACAACGA GGTGGGGA	15435
1882	CCACCACA A CAGGGCUU	6687	AAGCCCTG GGCTAGCTACAACGA TGTGGTGG	15436
1877	ACAACAGG G CUUGGGGU	6688	ACCCCAAG GGCTAGCTACAACGA CCTGTTGT	15437
1870	GGCUUGGG G UGAAGCAA	6689	TTGCTTCA GGCTAGCTACAACGA CCCAAGCC	15438
1865	GGGGUGAA G CAAUACAC	6690	GTGTATTG GGCTAGCTACAACGA TTCACCCC	15439
1862	GUGAAGCA A UACACUGG	6691	CCAGTGTA GGCTAGCTACAACGA TGCTTCAC	15440
1860	GAAGCAAU A CACUGGAC	6692	GGTAGCTA GGCTAGCTACAACGA ATTGCTTC	15441
1858	AGCAUAUAC A CUGGACCA	6693	TGGTCCAG GGCTAGCTACAACGA GTATTGCT	15442
1853	UACACUGG A CCACAUAC	6694	GTATGTGG GGCTAGCTACAACGA CCAGTGTA	15443
1850	ACUGGACC A CAUACCGU	6695	CAGGTATG GGCTAGCTACAACGA GGTCCAGT	15444
1848	UGGACCAC A UACCUGCG	6696	CGCAGGTA GGCTAGCTACAACGA GTGGTCCA	15445
1846	GACCACAU A CCUGCGAU	6697	ATCGCAGG GGCTAGCTACAACGA ATGTGGTC	15446
1842	ACAUACCU G CGAUGCGG	6698	CCGCATCG GGCTAGCTACAACGA AGGTATGT	15447
1839	UACCUGCG A UGCGGGUA	6699	TACCCGCA GGCTAGCTACAACGA CGCAGGTA	15448
1837	CCUGCGAU G CGGUACG	6700	CGTACCCG GGCTAGCTACAACGA ATCGCAGG	15449
1833	CGAUGCGG G UACGAUAC	6701	GTATCGTA GGCTAGCTACAACGA CCGCATCG	15450
1831	AUGCGGGU A CGAUACCA	6702	TGGTATCG GGCTAGCTACAACGA ACCCGCAT	15451
1828	CGGGUACG A UACCACAC	6703	GTGTGGTA GGCTAGCTACAACGA CGTACCCG	15452
1826	GGUACGAU A CCACACGG	6704	CCGTGTGG GGCTAGCTACAACGA ATCGTACC	15453
1823	ACGAUACC A CACGGCCG	6705	CGGCCGTG GGCTAGCTACAACGA GGTATCGT	15454
1821	GAUACCAC A CGGCCGCG	6706	CGCGGCCG GGCTAGCTACAACGA GTGGTATC	15455
1818	ACCACACG G CCGCGGUG	6707	CACCGCGG GGCTAGCTACAACGA CGTGTGGT	15456
1815	ACACGGCC G CGGUGCGU	6708	ACGCACCG GGCTAGCTACAACGA GGCCGTGT	15457
1812	CGGCCGCG G UCGUAGU	6709	ACTACGCA GGCTAGCTACAACGA CGCGGCCG	15458
1810	GCCGCGGU G CGUAGUGC	6710	GCACTACG GGCTAGCTACAACGA ACCGCGGC	15459
1808	CGCGGUGC G UAGUGCCA	6711	TGGCACTA GGCTAGCTACAACGA GCACCGCG	15460
1805	GGUGCGUA G UGCCAGCA	6712	TGCTGGCA GGCTAGCTACAACGA TACGCACC	15461
1803	UGCGUAGU G CCAGCAAU	6713	ATTGCTGG GGCTAGCTACAACGA ACTACGCA	15462

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1796	UGCCAGCA A UAGGGCCU	6715	AGGCCCTA GGCTAGCTACAACGA TGCTGGCA	15464
1791	GCAAUAGG G CCUCUGGU	6716	ACCAGAGG GGCTAGCTACAACGA CGTATTGC	15465
1784	GGCCUCUG G UCCGAGUU	6717	AACTCGGA GGCTAGCTACAACGA CAGAGGCC	15466
1778	UGGUCCGA G UUGUGGCC	6718	GGCCACAA GGCTAGCTACAACGA TCGGACCA	15467
1775	UCCGAGUU G UGGCCUC	6719	GAGGGCCA GGCTAGCTACAACGA AACTCGGA	15468
1772	GAGUUGUG G CCCUCGGU	6720	ACCGAGGG GGCTAGCTACAACGA CACAACCTC	15469
1765	GGCCUCUG G UGUAGGUG	6721	CACCTACA GGCTAGCTACAACGA CGAGGGCC	15470
1763	CCCUCGGU G UAGGUGAU	6722	ATCACCTA GGCTAGCTACAACGA ACCGAGGG	15471
1759	CGGUGUAG G UGAUAGGA	6723	TCCTATCA GGCTAGCTACAACGA CTACACCG	15472
1756	UGUAGGUG A UAGGACCC	6724	GGGTCTTA GGCTAGCTACAACGA CACCTACA	15473
1751	GUGAUAGG A CCCACCCC	6725	GGGTGGGG GGCTAGCTACAACGA CCTATCAC	15474
1746	AGGACCCC A CCCUGAG	6726	CTCAGGGG GGCTAGCTACAACGA GGGTCTCT	15475
1738	ACCCUGA G CGAACUUG	6727	CAAGTTCT GGCTAGCTACAACGA TCAGGGGT	15476
1734	CUGAGCGA A CUUGUCAA	6728	TGACAAG GGCTAGCTACAACGA TCGCTCAG	15477
1730	GCGAACUU G UCAAUGGA	6729	TCCATTGA GGCTAGCTACAACGA AAGTTCGC	15478
1726	ACUUGUCA A UGGAGCGG	6730	CCGCTCCA GGCTAGCTACAACGA TGACAAGT	15479
1721	UCAUUGGA G CGGCAGCU	6731	AGCTGCCG GGCTAGCTACAACGA TCCATTGA	15480
1718	AUGGACG G CAGCUGGC	6732	GCGAGCTG GGCTAGCTACAACGA CGTCCAT	15481
1715	GAGCGCA G UGGCCAA	6733	TTGGCCAG GGCTAGCTACAACGA TGCCGCTC	15482
1711	GGCAGCUG G CCAAGCGC	6734	GCGCTTGG GGCTAGCTACAACGA CAGCTGCC	15483
1706	CUGGCCAA G CGCUGUGG	6735	CCACAGCG GGCTAGCTACAACGA TTGGCCAG	15484
1704	GGCCAAGC G CUGUGGGC	6736	GCCCACAG GGCTAGCTACAACGA GCTTGGCC	15485
1701	CAAGCGCU G UGGGCAUC	6737	GATGCCCA GGCTAGCTACAACGA AGCGCTTG	15486
1697	CGCUGUGG G CAUCCGGA	6738	TCCGGATG GGCTAGCTACAACGA CCACAGCG	15487
1695	CUGUGGGC A UCCGGACG	6739	CGTCCGGA GGCTAGCTACAACGA GCCCACAG	15488
1689	GCAUCCG A CGAGUUGA	6740	TCAACTCG GGCTAGCTACAACGA CCGGATGC	15489
1685	CCGACGA G UUGAACCU	6741	AGGTTCAA GGCTAGCTACAACGA TCGTCCGG	15490
1680	CGAGUUGA A CCUGUGUG	6742	CACACAGG GGCTAGCTACAACGA TCAACTCG	15491
1676	UUGAACCU G UGUGCAUA	6743	TATGCACA GGCTAGCTACAACGA AGGTTCAA	15492
1674	GAACCUGU G UGCAUAGA	6744	TCTATGCA GGCTAGCTACAACGA ACAGGTTT	15493
1672	ACCUGUGU G CAUAGAAC	6745	GTTCTATG GGCTAGCTACAACGA ACACAGGT	15494
1670	CUGUGUGC A UAGAACAG	6746	CTGTTCTA GGCTAGCTACAACGA GCACACAG	15495
1665	UGCAUAGA A CAGUGCAG	6747	CTGCACTG GGCTAGCTACAACGA TCTATGCA	15496
1662	AUAGAACA G UGCAGCAA	6748	TTGTGCA GGCTAGCTACAACGA TGTCTAT	15497
1660	AGAACAGU G CAGCAUUG	6749	CCTGCTG GGCTAGCTACAACGA ACTGTTCT	15498
1657	ACAGUGCA G CAAUGAAC	6750	GTTTATTG GGCTAGCTACAACGA TGCATGT	15499
1654	GUGCAGCA A UGAACCCG	6751	CGGGTTCA GGCTAGCTACAACGA TGCTGCAC	15500
1650	AGCAAUGA A CCCGUUU	6752	AAACCGGG GGCTAGCTACAACGA TCATTGCT	15501
1645	UGAACCCG G UUUGGAGG	6753	CCTCCAAA GGCTAGCTACAACGA CGGGTTCA	15502
1634	UGGAGGGA G UCAUUGCA	6754	TGCAATGA GGCTAGCTACAACGA TCCCTCCA	15503
1631	AGGGAGUC A UUGCAGUU	6755	AACTGCAA GGCTAGCTACAACGA GACTCCCT	15504
1628	GAGUCAUU G CAGUUCAG	6756	CTGAAGT GGCTAGCTACAACGA AATGACTC	15505
1625	UCAUUGCA G UUCAGGGC	6757	GCCCTGAA GGCTAGCTACAACGA TGCAATGA	15506
1618	AGUUCAGG G CAGUCCUG	6758	CAGGACTG GGCTAGCTACAACGA CCTGAAC	15507
1615	UCAGGGCA G UCCUGUUA	6759	TAACAGGA GGCTAGCTACAACGA TGCCCTGA	15508
1610	GCAGUCCU G UUAUUGUG	6760	CACATTAA GGCTAGCTACAACGA AGGACTGC	15509
1606	UCCUGUUA A UGUGCCAG	6761	CTGGCACA GGCTAGCTACAACGA TAACAGGA	15510
1604	CUGUUAU G UGCCAGCU	6762	AGCTGGCA GGCTAGCTACAACGA ATTAACAG	15511
1602	GUUAAUGU G CCAGCUGC	6763	GCAGCTGG GGCTAGCTACAACGA ACATTAAC	15512
1598	AUGUGCCA G CUGCCGUU	6764	AACGGCAG GGCTAGCTACAACGA TGGCACAT	15513
1595	UGCCAGCU G CCGUUGGU	6765	ACCAACGG GGCTAGCTACAACGA AGCTGGCA	15514
1592	CAGCUGCC G UUGGUGUU	6766	AACACCAA GGCTAGCTACAACGA GGCAGCTG	15515
1588	UGCCGUUG G UGUUAAUA	6767	TATTAACA GGCTAGCTACAACGA CAACGGCA	15516
1586	CCGUUGGU G UUAUAAG	6768	CTTATTAA GGCTAGCTACAACGA ACCAACGG	15517
1582	UGGUGUUA A UAAGCUGG	6769	CCAGCTTA GGCTAGCTACAACGA TAACACCA	15518

1578	GUUAAUAA G CUGGAUUAU	6770	ATATCCAG GGCTAGCTACAACGA TTATTAAC	15519
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1571	AGCUGGAU A UUCUGAGA	6772	TCTCAGAA GGCTAGCTACAACGA ATCCAGCT	15521
1563	AUUCUGAG A UGCUCCAG	6773	CTGGAGCA GGCTAGCTACAACGA CTCAGAAT	15522
1561	UCUGAGAU G CUCCAGAU	6774	ATCTGGAG GGCTAGCTACAACGA ATCTCAGA	15523
1554	UGCUCCAG A UGUAAAGA	6775	TCTTTACA GGCTAGCTACAACGA CTGGAGCA	15524
1552	CUCCAGAU G UAAAGAGG	6776	CCTCTTTA GGCTAGCTACAACGA ATCTGGAG	15525
1542	AAAGAGGG A UGCCACCC	6777	GGGTGGCA GGCTAGCTACAACGA CCCTCTTT	15526
1540	AGAGGGAU G CCACCCUA	6778	TAGGGTGG GGCTAGCTACAACGA ATCCCTCT	15527
1537	GGGAUGCC A CCUACUA	6779	TAGTAGGG GGCTAGCTACAACGA GGCATCCC	15528
1532	GCCACCCU A CUAGUGGU	6780	ACCACCTAG GGCTAGCTACAACGA AGGCTGGC	15529
1528	CCCUACUA G UGUGUGGG	6781	CCACACCA GGCTAGCTACAACGA TAGTAGGG	15530
1525	UACUAGUG G UGUGGCC	6782	GGGCCACA GGCTAGCTACAACGA CACTAGTA	15531
1523	CUAGUGGU G UGGCCUG	6783	CAGGGCCA GGCTAGCTACAACGA ACCACTAG	15532
1520	GUGGUGUG G CCCUGCGC	6784	GCGCAGGG GGCTAGCTACAACGA CACACCAC	15533
1515	GUGGCCCU G CGCCCCC	6785	GGGGGGCG GGCTAGCTACAACGA AGGGCCAC	15534
1513	GGCCUGC G CCCCCCU	6786	AGGGGGGG GGCTAGCTACAACGA GCAGGGCC	15535
1504	CCCCCCU G UCGUGUAG	6787	CTACACGA GGCTAGCTACAACGA AGGGGGGG	15536
1501	CCCCUGC G UGUAGGUG	6788	CACCTACA GGCTAGCTACAACGA GACAGGGG	15537
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1495	UCGUGUAG G UGUCCCCG	6790	CGGGGACA GGCTAGCTACAACGA CTACACGA	15539
1493	GUGUAGGU G UCCCCGUC	6791	GACGGGGA GGCTAGCTACAACGA ACCTACAC	15540
1487	GUGUCCCC G UCAACGCC	6792	GGCGTTGA GGCTAGCTACAACGA GGGGACAC	15541
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1481	CCGUCAAC G CCGGCAA	6794	TTTGCCGG GGCTAGCTACAACGA GTTGACGG	15543
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1470	GGCAAAGA G UAGCAUA	6796	TGATGCTA GGCTAGCTACAACGA TCTTTGCC	15545
1467	AAAGAGUA G CAUCACAA	6797	TTGTGATG GGCTAGCTACAACGA TACTCTTT	15546
1465	AGAGUAGC A UCACAAUC	6798	GATTGTGA GGCTAGCTACAACGA GCTACTCT	15547
1462	GUAGCAUC A CAAUCAAC	6799	GTTGATTG GGCTAGCTACAACGA GATGCTAC	15548
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1453	CAAUCAAC A CCUUAGCC	6802	GGCTAAGG GGCTAGCTACAACGA GTTGATTG	15551
1447	ACACCUUA G CCCAGUUC	6803	GAACTGGG GGCTAGCTACAACGA TAAGGTGT	15552
1442	UUAGCCCC G UUCCCCAC	6804	GTGGGGAA GGCTAGCTACAACGA TGGGCTAA	15553
1435	AGUUCCCC A CCAUGGAA	6805	TTCCATGG GGCTAGCTACAACGA GGGGAACT	15554
1432	UCCCCACC A UGGAUUA	6806	TTATTCCA GGCTAGCTACAACGA GGTGGGGA	15555
1427	ACCAUGGA A UAAUAGGC	6807	GCCTATTA GGCTAGCTACAACGA TCCATGGT	15556
1424	AUGGAUA A UAGGCAAG	6808	CTTGCCCTA GGCTAGCTACAACGA TATTCCAT	15557
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1415	UAGGCAAG G CCCGCCAG	6810	CTGGCGGG GGCTAGCTACAACGA CTGTCCTA	15559
1411	CAAGGCCG G CCAGGACU	6811	AGTCCTGG GGCTAGCTACAACGA GGGCCTTG	15560
1405	CCGCCAGG A CUCCCCAG	6812	CTGGGGAG GGCTAGCTACAACGA CCTGGCGG	15561
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1393	CCCAGUGG G CCCCCGCC	6814	GGCGGGGG GGCTAGCTACAACGA CCACTGGG	15563
1387	GGGCCCCC G CCACCAUG	6815	CATGGTGG GGCTAGCTACAACGA GGGGGCCC	15564
1384	CCCCCGCC A CCAUGUCC	6816	GGACATGG GGCTAGCTACAACGA GGCGGGGG	15565
1381	CCGCCACC A UGUCCACG	6817	CGTGGACA GGCTAGCTACAACGA GGTGGCGG	15566
1379	GCCACCAU G UCCACGAC	6818	GTCGTGGA GGCTAGCTACAACGA ATGGTGGC	15567
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1372	GUUCCACG A CGGCUUGU	6820	ACAAGCCG GGCTAGCTACAACGA CGTGGACA	15569
1369	CCACGACG G CUUGUGGG	6821	CCCACAGG GGCTAGCTACAACGA CGTCGTGG	15570
1365	GACGGCUU G UGGGAUCC	6822	GGATCCCA GGCTAGCTACAACGA AAGCCGTC	15571
1360	CUUGUGGG A UCCGGAGC	6823	GCTCCGGA GGCTAGCTACAACGA CCCACAAG	15572
1353	GAUCCGGA G CAACUGCG	6824	CGCAGTTG GGCTAGCTACAACGA TCCGGATC	15573
1350	CCGGAGCA A CUGCGAUA	6825	TATCGCAG GGCTAGCTACAACGA TGCTCCGG	15574

1347	GAGCAACU G CGAUACCA	6826	TGGTATCG GGCTAGCTACAACGA AGTTGCTC	15575
1344	CAACUGCG A UACCACUA	6827	TAGTGGTA GGCTAGCTACAACGA CGCAGTTG	15576
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1339	GCGAUACC A CUAGGGCU	6829	AGCCCTAG GGCTAGCTACAACGA GGTATCGC	15578
1333	CCACUAGG G CUGUUGUA	6830	TACAACAG GGCTAGCTACAACGA CCTAGTGG	15579
1330	CUAGGGCU G UUGUAGGU	6831	ACCTACAA GGCTAGCTACAACGA AGCCCTAG	15580
1327	GGGUGUU G UAGGUGAC	6832	GTCACCTA GGCTAGCTACAACGA AACAGCCC	15581
1323	UGUUGUAG G UGACCAAU	6833	ATTGGTCA GGCTAGCTACAACGA CTACAACA	15582
1320	UGUAGGUG A CCAAUUCA	6834	TGAATTGG GGCTAGCTACAACGA CACCTACA	15583
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1312	ACCAAUUC A UCAUCAUA	6836	TATGATGA GGCTAGCTACAACGA GAATTGGT	15585
1309	AAUUCAUC A UCAUAUCC	6837	GGATATGA GGCTAGCTACAACGA GATGAATT	15586
1306	UCAUCAUC A UAUCCCAA	6838	TTGGGATA GGCTAGCTACAACGA GATGATGA	15587
1304	AUCAUCAU A UCCCAAGC	6839	GCTTGGGA GGCTAGCTACAACGA ATGATGAT	15588
1297	UAUCCCAA G CCAUGCGA	6840	TCGCATGG GGCTAGCTACAACGA TTGGGATA	15589
1294	CCCAAGCC A UGCGAUGG	6841	CCATCGCA GGCTAGCTACAACGA GGCTTGGG	15590
1292	CAAGCCAU G CGAUGGCC	6842	GGCCATCG GGCTAGCTACAACGA ATGGCTTG	15591
1289	GCCAUGCG A UGGCCUGA	6843	TCAGGCCA GGCTAGCTACAACGA CGCATGGC	15592
1286	AUGCGAUG G CCUGAUAC	6844	GTTACAGG GGCTAGCTACAACGA CATCGCAT	15593
1281	AUGGCCUG A UACGUGGC	6845	GCCACGTA GGCTAGCTACAACGA CAGGCCAT	15594
1279	GGCCUGAU A CGUGGCCG	6846	CGGCCACG GGCTAGCTACAACGA ATCAGGCC	15595
1277	CCUGAUAC G UGGCCGGG	6847	CCCGGCCA GGCTAGCTACAACGA GTATCAGG	15596
1274	GAUACGUG G CCGGGAUA	6848	TATCCCGG GGCTAGCTACAACGA CACGTATC	15597
1268	UGGCCGGG A UAGAUCGA	6849	TCGATCTA GGCTAGCTACAACGA CCCGGCCA	15598
1264	CGGGAUAG A UCGAGCAA	6850	TTGCTCGA GGCTAGCTACAACGA CTATCCCG	15599
1259	UAGAUCGA G CAAUUACA	6851	TGTAATTG GGCTAGCTACAACGA TCGATCTA	15600
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1253	GAGCAAUU A CAGUCCUG	6853	CAGGACTG GGCTAGCTACAACGA AATTGCTC	15602
1250	CAAUUACA G UCCUGUAC	6854	GTACAGGA GGCTAGCTACAACGA TGTAATTG	15603
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1243	AGUCCUGU A CUGUCUCA	6856	TGAGACAG GGCTAGCTACAACGA ACAGGACT	15605
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1216	GCGAGAAG G UGAACAGC	6862	GCTGTTCA GGCTAGCTACAACGA CTCTCGC	15611
1212	GAAGGUGA A CAGCUGAG	6863	CTCAGCTG GGCTAGCTACAACGA TCACCTTC	15612
1209	GGUGAACA G CUGAGAGA	6864	TCTCTCAG GGCTAGCTACAACGA TGTTCAAC	15613
1201	GCUGAGAG A CGAGGAAG	6865	CTTCTCTG GGCTAGCTACAACGA CTCTCAGC	15614
1192	CGAGGAAG A CAGAUCCG	6866	CGGATCTG GGCTAGCTACAACGA CTCTCTCG	15615
1188	GAAGACAG A UCCGCAGA	6867	TCTGCGGA GGCTAGCTACAACGA CTGTCTTC	15616
1184	ACAGAUCG G CAGAGAUC	6868	GATCTCTG GGCTAGCTACAACGA GGATCTGT	15617
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1169	UCCCCCAC G UACAUAGC	6871	GCTATGTA GGCTAGCTACAACGA GTGGGGGA	15620
1167	CCCCACGU A CAUAGCAG	6872	CTGCTATG GGCTAGCTACAACGA ACGTGGGG	15621
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1134	CCCAACGA G CAAAUCCA	6880	TCGATTTG GGCTAGCTACAACGA TCGTTGGG	15629
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1116	GUGACGCC G UAUCGUCG	6886	CGACGATA GGCTAGCTACAACGA GGCGTCAC	15635
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1105	UCGUCGUA G UGGGGAUG	6890	CATCCCCA GGCTAGCTACAACGA TACGACGA	15639
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1097	GUGGGGAU G CUGGCAUU	6892	AATGCCAG GGCTAGCTACAACGA ATCCCCAC	15641
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1084	CAUUCUG G CCGCGAGC	6895	GCTCGCGG GGCTAGCTACAACGA CAGGAATG	15644
1081	UCCUGGCC G CGAGCGUG	6896	CACGCTCG GGCTAGCTACAACGA GGCCAGGA	15645
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981	UGCCUCAU A CACAAUGC	6922	GCATTGTG GGCTAGCTACAACGA ATGAGGCA	15671
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974	UACACAAU G CUUGAGUU	6925	AACTCAAG GGCTAGCTACAACGA ATTGTGTA	15674
968	AUGCUUGA G UUGGAGCA	6926	TGCTCCAA GGCTAGCTACAACGA TCAAGCAT	15675
962	GAGUUGGA G CAAUCGUU	6927	AACGATTG GGCTAGCTACAACGA TCCAACCTC	15676
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956	GAGCAAUC G UUCGUGAC	6929	GTCACGAA GGCTAGCTACAACGA GATTGCTC	15678
952	AAUCGUUC G UGACAUGG	6930	CCATGTCA GGCTAGCTACAACGA GAACGATT	15679
949	CGUUCGUG A CAUGGUAC	6931	GTACCATG GGCTAGCTACAACGA CACGAACG	15680
947	UUCGUGAC A UGGUACAG	6932	CTGTACCA GGCTAGCTACAACGA GTCACGAA	15681
944	GUGACAU G UACAGCCC	6933	GGCTGTA GGCTAGCTACAACGA CATGTAC	15682
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939	AUGGUACA G CCCGGACG	6935	CGTCCGGG GGCTAGCTACAACGA TGTACCAT	15684
933	CAGCCCGG A CGCGUUGC	6936	GCAACGCG GGCTAGCTACAACGA CCGGGCTG	15685
931	GCCCGGAC G CGUUGCAC	6937	GTGCAACG GGCTAGCTACAACGA GTCCGGGC	15686

929	CCGGACGC G UUGCACAC	6938	GTGTGCAA GGCTAGCTACAACGA GCGTCCGG	15687
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924	CGCGUUGC A CACCUCAU	6940	ATGAGGTG GGCTAGCTACAACGA GCAACGCG	15689
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917	CACACCUC A UAAGCGGA	6942	TCCGCTTA GGCTAGCTACAACGA GAGGTGTG	15691
913	CCUCAUAA G CGGAGGCU	6943	AGCCTCCG GGCTAGCTACAACGA TTATGAGG	15692
907	AAGCGGAG G CUGGGAUG	6944	CATCCCGG GGCTAGCTACAACGA CTCCGCTT	15693
901	AGGCUGGG A UGGUCAGA	6945	TCTGACCA GGCTAGCTACAACGA CCCAGCCT	15694
898	CUGGGAUG G UCAGACAG	6946	CTGTCTGA GGCTAGCTACAACGA CATCCCGG	15695
893	AUGGUCAG A CAGGGCAG	6947	CTGCCCTG GGCTAGCTACAACGA CTGACCAT	15696
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857	GAGAAAGA G CAACCGGG	6952	CCCGGTTG GGCTAGCTACAACGA TCTTCTCT	15701
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849	GCAACCGG G CAGAUUCC	6954	GGAACTCT GGCTAGCTACAACGA CCGGTTGC	15703
845	CCGGGCAG A UUCCUGU	6955	ACAGGGAA GGCTAGCTACAACGA CTGCCCGG	15704
838	GAUUCUUU G UUGCAUAG	6956	CTATGCAA GGCTAGCTACAACGA AGGGAATC	15705
835	UCCUGUUU G CAUAGUUC	6957	GAAGTATG GGCTAGCTACAACGA AACAGGGA	15706
833	CCUGUUGC A UAGUUCAC	6958	GTGAACTA GGCTAGCTACAACGA GCAACAGG	15707
830	GUUGCAUA G UUCACGCC	6959	GGCGTGAA GGCTAGCTACAACGA TATGCAAC	15708
826	CAUAGUUC A CGCCGUCU	6960	AGACGGCG GGCTAGCTACAACGA GAAGTATG	15709
824	UAGUUCAC G CCGUCUUC	6961	GAAGACGG GGCTAGCTACAACGA GTGAACTA	15710
821	UUCACGCC G UCUUCCAG	6962	CTGGAAGA GGCTAGCTACAACGA GGCCTGAA	15711
811	CUUCCAGA A CCCGGACG	6963	CGTCCGGG GGCTAGCTACAACGA TCTGGAAG	15712
805	GAACCCGG A CGCCAUGC	6964	GCATGGCG GGCTAGCTACAACGA CCGGTTTC	15713
803	ACCCGGAC G CCAUGCGC	6965	GCGCATGG GGCTAGCTACAACGA GTCCGGGT	15714
800	CGGACGCC A UGCGCCAG	6966	CTGGCGCA GGCTAGCTACAACGA GGCCTCCG	15715
798	GACGCCAU G CGCCAGGG	6967	CCCTGGCG GGCTAGCTACAACGA ATGGCGTC	15716
796	CGCCAUGC G CAGGGGCC	6968	GGCCCTGG GGCTAGCTACAACGA GCATGGCG	15717
790	GCGCCAGG G CCCUGGCA	6969	TGCCAGGG GGCTAGCTACAACGA CCTGGCGC	15718
784	GGGCCCUG G CAGUGCCU	6970	AGGCACTG GGCTAGCTACAACGA CAGGGCCC	15719
781	CCCUGGCA G UGCCUCCC	6971	GGGAGGCA GGCTAGCTACAACGA TGCCAGGG	15720
779	CUGGCAGU G CCUCCCAA	6972	TTGGGAGG GGCTAGCTACAACGA ACTGCCAG	15721
766	CCAAGGGG G CGCCGACG	6973	CGTCGGCG GGCTAGCTACAACGA CCTCTTGG	15722
764	AAGGGGGC G CCGACGAG	6974	CTCGTCGG GGCTAGCTACAACGA GCCCCTTT	15723
760	GGGCGCCG A CGAGCGGA	6975	TCCGCTCG GGCTAGCTACAACGA CGGCGCCC	15724
756	GCCGACGA G CGGAAUGU	6976	ACATTCCG GGCTAGCTACAACGA TCGTCGGC	15725
751	CGAGCGGA A UGUACCCC	6977	GGGGTACA GGCTAGCTACAACGA TCCGCTCG	15726
749	AGCGGAAU G UACCCCAU	6978	ATGGGGTA GGCTAGCTACAACGA ATTCCGCT	15727
747	CGGAAUGU A CCCC AUGA	6979	TCATGGGG GGCTAGCTACAACGA ACATTCCG	15728
742	UGUACCCC A UGAGGUCG	6980	CGACCTCA GGCTAGCTACAACGA GGGGTACA	15729
737	CCCAUGAG G UCGGCGAA	6981	TTCGCGGA GGCTAGCTACAACGA CTCATGGG	15730
733	UGAGGUCG G CGAAGCCG	6982	CGGCTTCG GGCTAGCTACAACGA CGACCTCA	15731
728	UCGGCGAA G CCGCAUGU	6983	ACATGCGG GGCTAGCTACAACGA TTCGCGCA	15732
725	GCGAAGCC G CAUGUGAG	6984	CTCACATG GGCTAGCTACAACGA GGCTTCGC	15733
723	GAAGCCGC A UGUGAGGG	6985	CCCTCACA GGCTAGCTACAACGA GCGGCTTC	15734
721	AGCCGCAU G UGAGGGUA	6986	TACCCTCA GGCTAGCTACAACGA ATGCGGCT	15735
715	AUGUGAGG G UAUCGAUG	6987	CATCGATA GGCTAGCTACAACGA CCTCACAT	15736
713	GUGAGGGU A UCGAUGAC	6988	GTCATCGA GGCTAGCTACAACGA ACCCTCAC	15737
709	GGGUUAUCG A UGACCUUA	6989	TAAGTCA GGCTAGCTACAACGA CGATACCC	15738
706	UAUCGAUG A CCUUAACC	6990	GGGTAAGG GGCTAGCTACAACGA CATCGATA	15739
701	AUGACCUU A CCCAAGUU	6991	AACTTGGG GGCTAGCTACAACGA AAGGTCAT	15740
695	UUACCCAA G UUACGCGA	6992	TCGCGTAA GGCTAGCTACAACGA TTGGGTAA	15741
692	CCCAAGUU A CGCGACCU	6993	AGGTCGCG GGCTAGCTACAACGA AACTTGGG	15742

690	CAAGUUAC G CGACCUAC	6994	GTAGGTCG GGCTAGCTACAACGA GTAACCTG	15743
687	GUUACGCG A CCUACGCC	6995	GGCGTAGG GGCTAGCTACAACGA CGCGTAAC	15744
683	CGCGACCU A CGCCGGGG	6996	CCCCGGCG GGCTAGCTACAACGA AGGTCCGC	15745
681	CGACCUAC G CCGGGGGU	6997	ACCCCGCG GGCTAGCTACAACGA GTAGGTCG	15746
674	CGCCGGGG G UCCGUGGG	6998	CCCACGGA GGCTAGCTACAACGA CCCCGGCG	15747
670	GGGGGUCC G UGGGGCCC	6999	GGGCCCA GGCTAGCTACAACGA GGACCCC	15748
665	UCCGUGGG G CCCAACU	7000	AGTTGGGG GGCTAGCTACAACGA CCCACGGA	15749
659	GGGCCCCA A CUAGGCCG	7001	CGGCCTAG GGCTAGCTACAACGA TGGGGCCC	15750
654	CCAACUAG G CCGGGAGC	7002	GCTCCCGG GGCTAGCTACAACGA CTAGTTGG	15751
647	GGCCGGGA G CCGCGGGG	7003	CCCCGCGG GGCTAGCTACAACGA TCCCGGCC	15752
644	CGGGAGCG G CCGGGUGA	7004	TCACCCCG GGCTAGCTACAACGA GGCTCCCG	15753
639	GCCGCGGG G UGACAGGA	7005	TCCTGTCA GGCTAGCTACAACGA CCCGCGGC	15754
636	GCGGGGUG A CAGGAGCC	7006	GGCTCCTG GGCTAGCTACAACGA CACCCCGC	15755
630	UGACAGGA G CCAUCCUG	7007	CAGGATGG GGCTAGCTACAACGA TCCTGTCA	15756
627	CAGGAGCC A UCCUGCCC	7008	GGGCAGGA GGCTAGCTACAACGA GGCTCCTG	15757
622	GCAUCCU G CCCACCCU	7009	AGGGTGGG GGCTAGCTACAACGA AGGATGGC	15758
618	UCCUGCCC A CCCUAAGC	7010	GCTTAGGG GGCTAGCTACAACGA GGGCAGGA	15759
611	CACCCUAA G CCCUCAU	7011	AATGAGGG GGCTAGCTACAACGA TTAGGGTG	15760
605	AAGCCCUC A UUGCCAUA	7012	TATGGCAA GGCTAGCTACAACGA GAGGGCTT	15761
602	CCCUCAU G CCAUAGAG	7013	CTCTATGG GGCTAGCTACAACGA AATGAGGG	15762
599	UCAUUGCC A UAGAGGGG	7014	CCCCTCTA GGCTAGCTACAACGA GGCAATGA	15763
591	AUAGAGGG G CCAAGGGU	7015	ACCCTTGG GGCTAGCTACAACGA CCCTCTAT	15764
584	GGCCAAGG G UACCCGGG	7016	CCCGGGTA GGCTAGCTACAACGA CCTTGGCC	15765
582	CCAAGGGU A CCCGGGCU	7017	AGCCCGGG GGCTAGCTACAACGA ACCCTTGG	15766
576	GUACCCGG G CUGAGCCC	7018	GGGCTCAG GGCTAGCTACAACGA CCGGGTAC	15767
571	CGGGCUGA G CCCAGGCC	7019	GGCCTGGG GGCTAGCTACAACGA TCAGCCCG	15768
565	GAGCCCAG G CCCUGCCC	7020	GGGCAGGG GGCTAGCTACAACGA CTGGGCTC	15769
560	CAGGCCCU G CCCUCGGG	7021	CCCGAGGG GGCTAGCTACAACGA AGGGCTTG	15770
552	GCCCUCGG G CCGGCGAG	7022	CTCGCCGG GGCTAGCTACAACGA CCGAGGGC	15771
548	UCGGGCCG G CGAGCCUU	7023	AAGGCTCG GGCTAGCTACAACGA CGGCCCGA	15772
544	GCCGGCGA G CCUUGGGG	7024	CCCAAGG GGCTAGCTACAACGA TCGCCGGC	15773
535	CCUUGGGG A UAGGUUGU	7025	ACAACCTA GGCTAGCTACAACGA CCCAAGG	15774
531	GGGGAUAG G UUGUCGCC	7026	GGCGACAA GGCTAGCTACAACGA CTATCCCC	15775
528	GAUAGGUU G UCGCCUUC	7027	GAAGGCGA GGCTAGCTACAACGA AACCTATC	15776
525	AGGUUGUC G CCUUCCAC	7028	GTGGAAGG GGCTAGCTACAACGA GACAACCT	15777
518	CGCCUUC A CGAGGUUG	7029	CAACCTCG GGCTAGCTACAACGA GGAAGGCG	15778
513	UCCACGAG G UUGCGACC	7030	GGTCGCAA GGCTAGCTACAACGA CTCGTGGA	15779
510	ACGAGGUU G CGACGCGU	7031	AGCGGTCTG GGCTAGCTACAACGA AACCTCGT	15780
507	AGGUUGCG A CCGCUCGG	7032	CCGAGCGG GGCTAGCTACAACGA CGCAACCT	15781
504	UUGCGACC G CUCGGAAG	7033	CTTCCGAG GGCTAGCTACAACGA GGTCGCAA	15782
496	GCUCGGAA G UCUUCCUA	7034	TAGGAAGA GGCTAGCTACAACGA TTCCGAGC	15783
487	UCUUCCUA G UCGCGCGC	7035	GCGCGCGA GGCTAGCTACAACGA TAGGAAGA	15784
484	UCCUAGUC G CGCGCACA	7036	TGTGCGCG GGCTAGCTACAACGA GACTAGGA	15785
482	CUAGUCGC G CGCACACC	7037	GGTGTGCG GGCTAGCTACAACGA GCGACTAG	15786
480	AGUCGCGC G CACACCCA	7038	TGGGTGTG GGCTAGCTACAACGA GCGCGACT	15787
478	UCGCGCGC A CACCAAC	7039	GTTGGGTG GGCTAGCTACAACGA GCGCGCGA	15788
476	GCGCGCAC A CCCAACCU	7040	AGGTTGGG GGCTAGCTACAACGA GTGCGCGC	15789
471	CACACCCA A CCUGGGGC	7041	GCCCCAGG GGCTAGCTACAACGA TGGGTGTG	15790
464	AACCUGGG G CCCUGCG	7042	CGCAGGGG GGCTAGCTACAACGA CCCAGGTT	15791
458	GGGCCCCU G CGCGGCAA	7043	TTGCCGCG GGCTAGCTACAACGA AGGGGGCC	15792
456	GCCCCUGC G CGGCAACA	7044	TGTTGCCG GGCTAGCTACAACGA GCAGGGGC	15793
453	CCUGCGCG G CAACAGGU	7045	ACCTGTGG GGCTAGCTACAACGA CGCGCAGG	15794
450	GCGCGGCA A CAGUAAA	7046	TTTACCTG GGCTAGCTACAACGA TGCGCGC	15795
446	GGCAACAG G UAAACUCC	7047	GGAGTTTA GGCTAGCTACAACGA CTGTTGCC	15796
442	ACAGGUAA A CUCCACCA	7048	TGGTGGAG GGCTAGCTACAACGA TTACCTGT	15797
437	UAAACUCC A CCAACGAU	7049	ATCGTTGG GGCTAGCTACAACGA GGAGTTTA	15798

433	CUCCACCA A CGAUCUGA	7050	TCAGATCG GGCTAGCTACAACGA TGGTGGAG	15799
430	CACCAACG A UCUGACCA	7051	TGGTCAGA GGCTAGCTACAACGA CGTTGGTG	15800
425	ACGAUCUG A CCACCGCC	7052	GGCGGTGG GGCTAGCTACAACGA CAGATCGT	15801
422	AUCUGACC A CCGCCCGG	7053	CCGGGCGG GGCTAGCTACAACGA GGTCAGAT	15802
419	UGACCACC G CCCGGGAA	7054	TTCCCGGG GGCTAGCTACAACGA GGTGGTCA	15803
411	GCCCGGGA A CUUGACGU	7055	ACGTCAAG GGCTAGCTACAACGA TCCCGGGC	15804
406	GGAACUUG A CGUCCUGU	7056	ACAGGACG GGCTAGCTACAACGA CAAGTTCC	15805
404	AACUUGAC G UCCUGUGG	7057	CCACAGGA GGCTAGCTACAACGA GTCAAGTT	15806
399	GACGUCCU G UGGGCGGC	7058	GCCGCCCA GGCTAGCTACAACGA AGGACGTC	15807
395	UCCUGUGG G CGGCGGUU	7059	AACCGCCG GGCTAGCTACAACGA CCACAGGA	15808
392	UGUGGGCG G CGGUUGGU	7060	ACCAACCG GGCTAGCTACAACGA CGCCACAA	15809
389	GGGCGGCG G UUGGUGUU	7061	AACACCAA GGCTAGCTACAACGA CGCCGCC	15810
385	GGCGGUUG G UGUUACGU	7062	ACGTAACA GGCTAGCTACAACGA CAACCGCC	15811
383	CGGUUGGU G UUACGUUU	7063	AAACGTAA GGCTAGCTACAACGA ACCAACCG	15812
380	UUGGUGUU A CGUUUGGU	7064	ACCAAACG GGCTAGCTACAACGA AACACCAA	15813
378	GGUGUUAC G UUUGGUUU	7065	AAACCAAA GGCTAGCTACAACGA GTAACACC	15814
373	UACGUUUG G UUUUUCUU	7066	AAGAAAAA GGCTAGCTACAACGA CAAACGTA	15815
360	UCUUUGAG G UUUAGGAU	7067	ATCCTAAA GGCTAGCTACAACGA CTCAAAGA	15816
353	GGUUUAGG A UUCGUGCU	7068	AGCACGAA GGCTAGCTACAACGA CCTAAACC	15817
349	UAGGAUUC G UGCUCAUG	7069	CATGAGCA GGCTAGCTACAACGA GAATCCTA	15818
347	GGAUUCGU G CUCAUGGU	7070	ACCATGAG GGCTAGCTACAACGA ACGAATCC	15819
343	UCGUGCUC A UGGUGCAC	7071	GTGCACCA GGCTAGCTACAACGA GAGCACGA	15820
340	UGCUC AUG G UGCACGGU	7072	ACCGTGCA GGCTAGCTACAACGA CATGAGCA	15821
338	CUCAUGGU G CACGGUCU	7073	AGACCGTG GGCTAGCTACAACGA ACCATGAG	15822
336	CAUGGUGC A CGGUCUAC	7074	GTAGACCG GGCTAGCTACAACGA GCACCATG	15823
333	GGUGCACG G UCUACGAG	7075	CTCGTAGA GGCTAGCTACAACGA CGTGCACC	15824
329	CACGGUCU A CGAGACCU	7076	AGGTCTCG GGCTAGCTACAACGA AGACCGTG	15825
324	UCUACGAG A CCUCCCGG	7077	CCGGGAGG GGCTAGCTACAACGA CCGCTAGA	15826
314	CUCCCGGG G CACUCGCA	7078	TGCGAGTG GGCTAGCTACAACGA CCGGGGAG	15827
312	CCCGGGGG A CUCGCAAG	7079	CTTGCGAG GGCTAGCTACAACGA GCCCGGGG	15828
308	GGGCACUC G CAAGCACC	7080	GGTGCTTG GGCTAGCTACAACGA GAGTGCCC	15829
304	ACUCGCAA G CACCCUAU	7081	ATAGGGTG GGCTAGCTACAACGA TTGCGAGT	15830
302	UCGCAAGC A CCCUAUCA	7082	TGATAGGG GGCTAGCTACAACGA GCTTGCGA	15831
297	AGCACCCU A UCAGGCAG	7083	CTGCCTGA GGCTAGCTACAACGA AGGGTGCT	15832
292	CCUAUCAG G CAGUACCA	7084	TGTGACTG GGCTAGCTACAACGA CTGATAGG	15833
289	AUCAGGCA G UACCACAA	7085	TTGTGGTA GGCTAGCTACAACGA TGCCTGAT	15834
287	CAGGCAGU A CCACAAGG	7086	CCTTGTGG GGCTAGCTACAACGA ACTGCCTG	15835
284	GCAGUACC A CAAGGCCU	7087	AGGCCTTG GGCTAGCTACAACGA GGTACTGC	15836
279	ACCACAAG G CCUUUCGC	7088	GCGAAAGG GGCTAGCTACAACGA CTTGTGGT	15837
272	GGCCUUUC G CGACCCAA	7089	TTGGGTGC GGCTAGCTACAACGA GAAAGGCC	15838
269	CUUUCGCG A CCCAACAC	7090	GTGTTGGG GGCTAGCTACAACGA CGCGAAAG	15839
264	GCGACCCA A CACUACUC	7091	GAGTAGTG GGCTAGCTACAACGA TGGGTGCG	15840
262	GACCCAAC A CUACUCGG	7092	CCGAGTAG GGCTAGCTACAACGA GTTGGGTC	15841
259	CCAACACU A CUCGGCUA	7093	TAGCCGAG GGCTAGCTACAACGA AGTGTGG	15842
254	ACUACUCG G CUAGCAGU	7094	ACTGCTAG GGCTAGCTACAACGA CGAGTAGT	15843
250	CUCGGCUA G CAGUCUCG	7095	CGAGACTG GGCTAGCTACAACGA TAGCCGAG	15844
247	GGCUAGCA G UCUCGCGG	7096	CCGCGAGA GGCTAGCTACAACGA TGCTAGCC	15845
242	GCAGUCUC G CGGGGGCA	7097	TGCCCCCG GGCTAGCTACAACGA GAGACTGC	15846
236	UCGCGGGG G CACGCCCA	7098	TGGGCGTG GGCTAGCTACAACGA CCCC CGCA	15847
234	GCGGGGGG A CGCCCAA	7099	TTTGGGCG GGCTAGCTACAACGA GCCCCGCG	15848
232	GGGGGGAC A CCAAAUUC	7100	GATTTGGG GGCTAGCTACAACGA GTGCCCC	15849
226	ACGCCCAA A UCUCGAG	7101	CCTGGAGA GGCTAGCTACAACGA TTGGCGGT	15850
218	AUCUCCAG G CAUUGAGC	7102	GCTCAATG GGCTAGCTACAACGA CTGGAGAT	15851
216	CUCCAGGC A UUGAGCGG	7103	CCGCTCAA GGCTAGCTACAACGA GCCTGGAG	15852
211	GGCAUUGA G CGGGUUGA	7104	TCAACCCG GGCTAGCTACAACGA TCAATGCC	15853
207	UUGAGCGG G UUGAUCCA	7105	TGGATCAA GGCTAGCTACAACGA CCGCTCAA	15854

203	GCGGGUUG A UCCAAGAA	7106	TTCTTGGA GGCTAGCTACAACGA CAACCCGC	15855
191	AAGAAAGG A CCCGGUCG	7107	CGACCGGG GGCTAGCTACAACGA CCTTTCTT	15856
186	AGGACCCG G UCGUCCUG	7108	CAGGACGA GGCTAGCTACAACGA CGGGTCCT	15857
183	ACCCGGUC G UCCUGGCA	7109	TGCCAGGA GGCTAGCTACAACGA GACCGGGT	15858
177	UCGUCCUG G CAAUCCG	7110	CGGAATTG GGCTAGCTACAACGA CAGGACGA	15859
174	UCCUGGCA A UUCCGGUG	7111	CACCGGAA GGCTAGCTACAACGA TGCCAGGA	15860
168	CAAUCCG G UGUACUCA	7112	TGAGTACA GGCTAGCTACAACGA CGGAATTG	15861
166	AUCCGGU G UACUCACC	7113	GGTGAGTA GGCTAGCTACAACGA ACCGGAAT	15862
164	UCCGGUGU A CUCACCGG	7114	CCGGTGAG GGCTAGCTACAACGA ACACCGGA	15863
160	GUGUACUC A CCGGUUCC	7115	GGAAACCG GGCTAGCTACAACGA GAGTACAC	15864
156	ACUACCG G UUCCGCAG	7116	GGCTCGGA GGCTAGCTACAACGA CGGTGAGT	15865
151	CCGGUUC G CAGACCAC	7117	GTGGTCTG GGCTAGCTACAACGA GGAACCGG	15866
147	UUCGCGAG A CCACUAUG	7118	CATAGTGG GGCTAGCTACAACGA CTGCGGAA	15867
144	CGCAGACC A CUAUGGCU	7119	AGCCATAG GGCTAGCTACAACGA GGTCTGCG	15868
141	AGACCACU A UGGCUCUC	7120	GAGAGCCA GGCTAGCTACAACGA AGTGGTCT	15869
138	CCACUAUG G CUCUCCCG	7121	CGGGAGAG GGCTAGCTACAACGA CATAGTGG	15870
120	GAGGGGGG G UCCUGGAG	7122	CTCCAGGA GGCTAGCTACAACGA CCCCCCTC	15871
111	UCCUGGAG G CUGCACGA	7123	TCGTGCAG GGCTAGCTACAACGA CTCCAGGA	15872
108	UGGAGGCC A CAGCACAC	7124	GTGTCGTG GGCTAGCTACAACGA AGCCTCCA	15873
106	GAGGCGC A CGACACUC	7125	GAGTGTCTG GGCTAGCTACAACGA GCAGCCTC	15874
103	GCUGCACG A CACUCAUA	7126	TATGAGTG GGCTAGCTACAACGA CGTGCAGC	15875
101	UGCACGAC A CUCAUACU	7127	AGTATGAG GGCTAGCTACAACGA GTCGTGCA	15876
97	CGACACUC A UACUACG	7128	CGTTAGTA GGCTAGCTACAACGA GAGTGTCTG	15877
95	ACACUCAU A CUAACGCC	7129	GGCGTTAG GGCTAGCTACAACGA ATGAGTGT	15878
91	UCAUACUA A CGCCAUGG	7130	CCATGGCG GGCTAGCTACAACGA TAGTATGA	15879
89	AUACUAAC G CCAUGGCU	7131	AGCCATGG GGCTAGCTACAACGA GTTAGTAT	15880
86	CUAACGCC A UGGCUAGA	7132	TCTAGCCA GGCTAGCTACAACGA GGCGTTAG	15881
83	ACGCCAUG G CUAGACGC	7133	GCGTCTAG GGCTAGCTACAACGA CATGGCGT	15882
78	AUGGCUAG A CGCUUUCU	7134	AGAAAGCG GGCTAGCTACAACGA CTAGCCAT	15883
76	GGCUAGAC G CUUUCUGC	7135	GCAGAAAG GGCTAGCTACAACGA GTCTAGCC	15884
69	CGCUUUCU G CGUGAAGA	7136	TCTTCACG GGCTAGCTACAACGA AGAAAGCG	15885
67	CUUUCUGC G UGAAGACA	7137	TGTCTTCA GGCTAGCTACAACGA GCAGAAAG	15886
61	GCGUGAAG A CAGUAGUU	7138	AACTACTG GGCTAGCTACAACGA CTTCACGC	15887
58	UGAAGACA G UAGUCCU	7139	AGGAACTA GGCTAGCTACAACGA TGTCTTCA	15888
55	AGACAGUA G UCCUCAC	7140	GTGAGGAA GGCTAGCTACAACGA TACTGTCT	15889
48	AGUCCUC A CAGGGGAG	7141	CTCCCCTG GGCTAGCTACAACGA GAGGAAC	15890
40	ACAGGGGA G UGAUCUAU	7142	ATAGATCA GGCTAGCTACAACGA TCCCCTGT	15891
37	GGGGAGUG A UCUAUGGU	7143	ACCATAGA GGCTAGCTACAACGA CACTCCCC	15892
33	AGUGAUCU A UGGUGGAG	7144	CTCCACCA GGCTAGCTACAACGA AGATCACT	15893
30	GAUCUAUG G UGGAGUGU	7145	ACACTCCA GGCTAGCTACAACGA CATAGATC	15894
25	AUGGUGGA G UGUCGCCC	7146	GGGCGACA GGCTAGCTACAACGA TCCACCAT	15895
23	GGUGGAGU G UCGCCCC	7147	GGGGGCGA GGCTAGCTACAACGA ACTCCACC	15896

Input Sequence = HPCK1S1. Cut Site = R/Y

Arm Length = 8. Core Sequence = GGCTAGCTACAACGA

HPCK1S1 Hepatitis C virus (strain HCV-1b, clone HCV-K1-S1), complete genome; acc#
gi|1030702|dbj|D50483.1; 9410 nt

Table XX: Synthetic anti-HCV nucleic acid molecule and Target Sequences

ref pos	Ref Seq	Target	Seq ID	RPI#	NUCLEIC ACID	Seq ID	Nucleic Acid Alias
195	HCV+	GGGUCCU U UCUUGGA	7148	15364	c ₅ c ₅ a ₅ a ₅ ga cUGAuGaggcgaaagccGaa Aggacc B	15897	Hammerhead
342	HCV+	AGACCGUGCAUGAGCAC	7149	17501	G ₅ ⁺ T ₅ G ₅ C ₅ T ₅ C ₅ A ₅ T ₅ G ₅ A ₅ C ₅ G ₅ T ₅ C ₅ T	15898	Antisense
195	HCV+	GGGUCCU U UCUUGGA	7148	17558	c ₅ c ₅ a ₅ a ₅ ga cUGAuGaggcguaagccGaz Aggacc B	15899	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	17559	c ₅ c ₅ a ₅ a ₅ ga cUGAuGaggcguaagccGaa AggaZc B	15900	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	17560	Z ₅ c ₅ a ₅ a ₅ ga cUGAuGaggcguaagccGaa Aggacc B	15901	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	17561	Z c ₅ a ₅ a ₅ ga cUGAuGaggcguaagccGaa Aggacc B	15902	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	18012	ccaaga cUGAuGaggcguaagccGaa Aggacc B	15903	Hammerhead
82	HCV+	GCGUCUA G CCAUGGC	7150	18744	G ₅ C ₅ C ₅ a ₅ ugg GccgaaagGCCGaGucuaaGGuCu uagacgc B	15904	Zinzyme
100	HCV+	AGUAUGA G UGUCGUG	7151	18745	c ₅ a ₅ c ₅ s ₅ aca GccgaaagGCCGaGucuaaGGuCu ucauacu B	15905	Zinzyme
102	HCV+	UAUGAGU G UCGUGCA	7152	18746	u ₅ g ₅ c ₅ s ₅ cga GccgaaagGCCGaGucuaaGGuCu acucaua B	15906	Zinzyme
105	HCV+	GAGUGUC G UGCAGCC	7153	18747	G ₅ G ₅ C ₅ u ₅ gca GccgaaagGCCGaGucuaaGGuCu gacacuc B	15907	Zinzyme
107	HCV+	GUGUGCU G CAGCCUC	7154	18748	G ₅ a ₅ g ₅ g ₅ cug GccgaaagGCCGaGucuaaGGuCu acgacac B	15908	Zinzyme
146	HCV+	CAUAGUG G UCUGCGG	7155	18749	c ₅ c ₅ g ₅ c ₅ saga GccgaaagGCCGaGucuaaGGuCu cacuaug B	15909	Zinzyme
190	HCV+	CGACCCG G UCCUUUC	7156	18750	G ₅ a ₅ a ₅ a ₅ gga GccgaaagGCCGaGucuaaGGuCu ccgguccg B	15910	Zinzyme
217	HCV+	GCUCAAU G CCUGGAG	7157	18751	C ₅ u ₅ C ₅ C ₅ agg GccgaaagGCCGaGucuaaGGuCu auugagc B	15911	Zinzyme
231	HCV+	GAUUUGG G CGUGCCC	7158	18752	G ₅ g ₅ g ₅ c ₅ acg GccgaaagGCCGaGucuaaGGuCu ccaaauc B	15912	Zinzyme
258	HCV+	UAGCCGA G UAGUGUU	7159	18753	a ₅ a ₅ c ₅ a ₅ sua GccgaaagGCCGaGucuaaGGuCu ucggcua B	15913	Zinzyme
307	HCV+	GGUGCUU G CGAGUGC	7160	18754	G ₅ c ₅ a ₅ s ₅ ucg GccgaaagGCCGaGucuaaGGuCu aagcacc B	15914	Zinzyme
77	HCV+	GAAAGC G UCUAGC	7161	18755	G ₅ C ₅ u ₅ a ₅ ga GccgaaagGCCGaGucuaaGGuCu gcuuuc B	15915	Zinzyme
77	HCV+	AGAAAGC G UCUAGCC	7162	18756	G ₅ g ₅ c ₅ u ₅ saga GccgaaagGCCGaGucuaaGGuCu gcuuuc B	15916	Zinzyme
88	HCV+	AGCAUG G CGUUAGU	7163	18757	a ₅ c ₅ u ₅ a ₅ sacg GccgaaagGCCGaGucuaaGGuCu cauggcu B	15917	Zinzyme
94	HCV+	GGCGUTUA G UAUGAGU	7164	18758	a ₅ c ₅ u ₅ C ₅ sua GccgaaagGCCGaGucuaaGGuCu uaacgcc B	15918	Zinzyme
102	HCV+	AUGAGU G UCGUGC	7165	18759	G ₅ c ₅ a ₅ C ₅ ga GccgaaagGCCGaGucuaaGGuCu acucau B	15919	Zinzyme
105	HCV+	AGUGUC G UGCAGC	7166	18760	G ₅ c ₅ u ₅ g ₅ sca GccgaaagGCCGaGucuaaGGuCu gacacu B	15920	Zinzyme
110	HCV+	UCGUGCA G CCUCCAG	7167	18761	C ₅ u ₅ g ₅ g ₅ agg GccgaaagGCCGaGucuaaGGuCu ugacaga B	15921	Zinzyme
137	HCV+	GGGAGA G CCAUAG	7168	18762	C ₅ u ₅ a ₅ u ₅ gg GccgaaagGCCGaGucuaaGGuCu ucuccc B	15922	Zinzyme
137	HCV+	CGGGAGA G CCAUAGU	7169	18763	a ₅ c ₅ u ₅ a ₅ ugg GccgaaagGCCGaGucuaaGGuCu ucucccg B	15923	Zinzyme
146	HCV+	AUAGUG G UCUGCG	7170	18764	c ₅ g ₅ c ₅ a ₅ ga GccgaaagGCCGaGucuaaGGuCu cacuaa B	15924	Zinzyme
150	HCV+	GUGGUCU G CGGAACC	7171	18765	G ₅ g ₅ u ₅ a ₅ ccg GccgaaagGCCGaGucuaaGGuCu agaccac B	15925	Zinzyme
176	HCV+	CGGAUUU G CCAGGAC	7172	18766	G ₅ u ₅ C ₅ C ₅ ugg GccgaaagGCCGaGucuaaGGuCu aauncg B	15926	Zinzyme

190	HCV+	GACGG G UCCUUU	7173	18767	a ₉ a ₉ a ₉ s ₉ ga	GccgaaagCCGaGucaaGGuCu	cgguc B	15927	Zinzyme
253	HCV+	CUGCUA G CCGAGU	7174	18768	a ₉ c ₉ u ₉ c ₉ gg	GccgaaagCCGaGucaaGGuCu	uagcag B	15928	Zinzyme
253	HCV+	ACUGCUA G CCGAGUA	7175	18769	u ₉ a ₉ c ₉ u ₉ c ₉ gg	GccgaaagCCGaGucaaGGuCu	uagcagu B	15929	Zinzyme
258	HCV+	AGCCGA G UAGUGU	7176	18770	a ₉ c ₉ a ₉ c ₉ s ₉ ua	GccgaaagCCGaGucaaGGuCu	ucggcu B	15930	Zinzyme
263	HCV+	GAGUAGU G UUGGGUC	7177	18771	g ₉ a ₉ c ₉ c ₉ s ₉ caa	GccgaaagCCGaGucaaGGuCu	acuacuc B	15931	Zinzyme
268	HCV+	UGUJUG G UCGCGA	7178	18772	u ₉ c ₉ g ₉ c ₉ s ₉ ga	GccgaaagCCGaGucaaGGuCu	ccaaca B	15932	Zinzyme
268	HCV+	GUGUJUG G UCGCGAA	7179	18773	u ₉ u ₉ c ₉ g ₉ c ₉ ga	GccgaaagCCGaGucaaGGuCu	ccaacac B	15933	Zinzyme
271	HCV+	UUGGGUC G CGAAAGG	7180	18774	c ₉ s ₉ c ₉ u ₉ s ₉ u ₉ c ₉ g	GccgaaagCCGaGucaaGGuCu	gacccaa B	15934	Zinzyme
283	HCV+	AGGCCUU G UGGUACU	7181	18775	a ₉ s ₉ u ₉ a ₉ s ₉ cca	GccgaaagCCGaGucaaGGuCu	aaggccu B	15935	Zinzyme
286	HCV+	CCUUGUG G UACUGCC	7182	18776	g ₉ g ₉ c ₉ a ₉ s ₉ gua	GccgaaagCCGaGucaaGGuCu	cacaagg B	15936	Zinzyme
291	HCV+	UGGUACU G CCUGAUA	7183	18777	u ₉ a ₉ u ₉ s ₉ c ₉ a ₉ gg	GccgaaagCCGaGucaaGGuCu	aguacca B	15937	Zinzyme
301	HCV+	UGAUAGG G UGCUUGC	7184	18778	g ₉ a ₉ c ₉ a ₉ a ₉ sgca	GccgaaagCCGaGucaaGGuCu	ccuauca B	15938	Zinzyme
303	HCV+	AUAGGGU G CUUGCGA	7185	18779	u ₉ c ₉ g ₉ c ₉ s ₉ a ₉ ag	GccgaaagCCGaGucaaGGuCu	accuau B	15939	Zinzyme
60	HCV+	ACUACU G UCUUCA	7186	18780	u ₉ g ₉ a ₉ s ₉ a ₉ sga	GccgaaagCCGaGucaaGGuCu	aguagu B	15940	Zinzyme
60	HCV+	AACUACU G UCUUCAC	7187	18781	g ₉ s ₉ g ₉ s ₉ a ₉ aga	GccgaaagCCGaGucaaGGuCu	aguaguu B	15941	Zinzyme
68	HCV+	UCUUCAC G CAGAAAG	7188	18782	c ₉ s ₉ u ₉ u ₉ s ₉ c ₉ ug	GccgaaagCCGaGucaaGGuCu	gugaaga B	15942	Zinzyme
75	HCV+	CAGAAA G CGUCUA	7189	18783	u ₉ a ₉ g ₉ a ₉ s ₉ c ₉ g	GccgaaagCCGaGucaaGGuCu	uuucug B	15943	Zinzyme
82	HCV+	CGUCUA G CCAUGG	7190	18784	c ₉ g ₉ a ₉ s ₉ u ₉ gg	GccgaaagCCGaGucaaGGuCu	uagacg B	15944	Zinzyme
88	HCV+	GCCAUG G CGUUAG	7191	18785	c ₉ s ₉ a ₉ s ₉ s ₉ c ₉ g	GccgaaagCCGaGucaaGGuCu	cauggc B	15945	Zinzyme
90	HCV+	CAUGGC G UUAGUA	7192	18786	u ₉ a ₉ c ₉ s ₉ u ₉ aa	GccgaaagCCGaGucaaGGuCu	gccaug B	15946	Zinzyme
90	HCV+	CCAUGGC G UUAGUAU	7193	18787	a ₉ u ₉ a ₉ c ₉ u ₉ aa	GccgaaagCCGaGucaaGGuCu	gccauug B	15947	Zinzyme
100	HCV+	GUAUGA G UGUCGU	7194	18788	a ₉ c ₉ g ₉ a ₉ s ₉ ca	GccgaaagCCGaGucaaGGuCu	ucauac B	15948	Zinzyme
107	HCV+	UGUCGU G CAGCCU	7195	18789	a ₉ g ₉ g ₉ c ₉ s ₉ ug	GccgaaagCCGaGucaaGGuCu	acgaca B	15949	Zinzyme
110	HCV+	CGUGCA G CCUCCA	7196	18790	u ₉ g ₉ g ₉ s ₉ a ₉ gg	GccgaaagCCGaGucaaGGuCu	ugcacg B	15950	Zinzyme
150	HCV+	UGGUUCU G CGGAAC	7197	18791	g ₉ u ₉ s ₉ c ₉ s ₉ c ₉ g	GccgaaagCCGaGucaaGGuCu	agacca B	15951	Zinzyme
159	HCV+	GGAACCG G UGAGUAC	7198	18792	g ₉ u ₉ a ₉ s ₉ u ₉ ca	GccgaaagCCGaGucaaGGuCu	cgguucc B	15952	Zinzyme
176	HCV+	GGAUUU G CCAGGA	7199	18793	u ₉ c ₉ c ₉ a ₉ u ₉ gg	GccgaaagCCGaGucaaGGuCu	aanuucc B	15953	Zinzyme
217	HCV+	CUCAAU G CCUGGA	7200	18794	u ₉ c ₉ c ₉ s ₉ a ₉ gg	GccgaaagCCGaGucaaGGuCu	auugag B	15954	Zinzyme
231	HCV+	AUUUGG G CGUGCC	7201	18795	g ₉ g ₉ c ₉ s ₉ a ₉ c ₉ g	GccgaaagCCGaGucaaGGuCu	ccaaau B	15955	Zinzyme
261	HCV+	CGAGUA G UGUUGG	7202	18796	c ₉ g ₉ a ₉ a ₉ s ₉ ca	GccgaaagCCGaGucaaGGuCu	uacucg B	15956	Zinzyme
261	HCV+	CCGAGUA G UGUUGGG	7203	18797	c ₉ s ₉ c ₉ s ₉ a ₉ aca	GccgaaagCCGaGucaaGGuCu	uacucgg B	15957	Zinzyme
263	HCV+	AGUAGU G UTUGGGU	7204	18798	a ₉ c ₉ c ₉ s ₉ caa	GccgaaagCCGaGucaaGGuCu	acuacu B	15958	Zinzyme
271	HCV+	UGGGUC G CGAAAG	7205	18799	c ₉ s ₉ u ₉ s ₉ u ₉ c ₉ g	GccgaaagCCGaGucaaGGuCu	gaccca B	15959	Zinzyme
283	HCV+	GGCCUU G UGGUAC	7206	18800	g ₉ u ₉ a ₉ c ₉ s ₉ ca	GccgaaagCCGaGucaaGGuCu	aaggcc B	15960	Zinzyme
291	HCV+	GGUACU G CCUGAU	7207	18801	a ₉ u ₉ c ₉ a ₉ s ₉ gg	GccgaaagCCGaGucaaGGuCu	aguacc B	15961	Zinzyme

303	HCV+	UAGGGU G CUUGCG	7208	18802	C ₅ G ₅ C ₅ A ₅ ag GccgaaagGCGaGucaaGGuCu acccua B	15962	Zinzyme
307	HCV+	GUGCTU G CGAGUG	7209	18803	C ₅ A ₅ C ₅ U ₅ CG GccgaaagGCGaGucaaGGuCu aagcac B	15963	Zinzyme
323	HCV+	CGGAG G UCUCGU	7210	18804	A ₅ C ₅ G ₅ A ₅ ga GccgaaagGCGaGucaaGGuCu cucccg B	15964	Zinzyme
323	HCV+	CCGGAG G UCUCGUA	7211	18805	U ₅ A ₅ C ₅ G ₅ A ₅ ga GccgaaagGCGaGucaaGGuCu cucccg B	15965	Zinzyme
75	HCV+	GCAGAAA G CGUCUAG	7212	18806	C ₅ U ₅ A ₅ G ₅ acg GccgaaagGCGaGucaaGGuCu uuucugc B	15966	Zinzyme
143	HCV+	GCCAU A G UGGUCU	7213	18807	A ₅ G ₅ A ₅ C ₅ ca GccgaaagGCGaGucaaGGuCu uauggc B	15967	Zinzyme
278	HCV+	GCGAAAG G CCUUGUG	7214	18808	C ₅ A ₅ C ₅ A ₅ agg GccgaaagGCGaGucaaGGuCu cuuucgc B	15968	Zinzyme
163	HCV+	CGGUA G UACACC	7215	18809	G ₅ G ₅ U ₅ G ₅ ua GccgaaagGCGaGucaaGGuCu ucaccg B	15969	Zinzyme
68	HCV+	CUUCAC G CAGAAA	7216	18810	U ₅ U ₅ U ₅ C ₅ ug GccgaaagGCGaGucaaGGuCu gugaag B	15970	Zinzyme
94	HCV+	GCGUUA G UAUGAG	7217	18811	C ₅ U ₅ C ₅ A ₅ ua GccgaaagGCGaGucaaGGuCu uaacgc B	15971	Zinzyme
143	HCV+	AGCCAU A G UGGUCUG	7218	18812	C ₅ A ₅ G ₅ A ₅ cca GccgaaagGCGaGucaaGGuCu uauggcu B	15972	Zinzyme
159	HCV+	GAACCG G UGAGUA	7219	18813	U ₅ A ₅ C ₅ U ₅ ca GccgaaagGCGaGucaaGGuCu cgguuc B	15973	Zinzyme
163	HCV+	CCGGUA G UACACCG	7220	18814	C ₅ G ₅ G ₅ U ₅ gua GccgaaagGCGaGucaaGGuCu ucaccgg B	15974	Zinzyme
249	HCV+	GAGACU G CUAGCC	7221	18815	G ₅ G ₅ C ₅ U ₅ ag GccgaaagGCGaGucaaGGuCu agucuc B	15975	Zinzyme
249	HCV+	CGAGACU G CUAGCCG	7222	18816	C ₅ G ₅ G ₅ C ₅ uag GccgaaagGCGaGucaaGGuCu agucucg B	15976	Zinzyme
278	HCV+	CGAAAG G CCUUGU	7223	18817	A ₅ C ₅ A ₅ A ₅ gg GccgaaagGCGaGucaaGGuCu cuuucg B	15977	Zinzyme
286	HCV+	CUUGUG G UACUGC	7224	18818	G ₅ C ₅ A ₅ G ₅ ua GccgaaagGCGaGucaaGGuCu cacaag B	15978	Zinzyme
301	HCV+	GAUAGG G UGUUG	7225	18819	C ₅ A ₅ A ₅ G ₅ ca GccgaaagGCGaGucaaGGuCu ccuauc B	15979	Zinzyme
328	HCV+	GGUCUC G UAGACC	7226	18820	G ₅ G ₅ U ₅ C ₅ ua GccgaaagGCGaGucaaGGuCu gagacc B	15980	Zinzyme
328	HCV+	AGGUCUC G UAGACCG	7227	18821	C ₅ G ₅ G ₅ U ₅ cua GccgaaagGCGaGucaaGGuCu gagaccu B	15981	Zinzyme
335	HCV+	UAGACC G UGCACC	7228	18822	G ₅ G ₅ U ₅ G ₅ ca GccgaaagGCGaGucaaGGuCu ggucua B	15982	Zinzyme
30	C	UAAACCU C AAAGAAA	7229	19108	U ₅ U ₅ U ₅ C ₅ uuu cUGAuGagggccguuagggccGaa Agguuua B	15983	Hammerhead
48	C	CAAAAGU A ACACCAA	7230	19109	U ₅ U ₅ G ₅ G ₅ ugu cUGAuGagggccguuagggccGaa Acguuug B	15984	Hammerhead
60	C	CAACCGU C GCCCACA	7231	19110	U ₅ G ₅ U ₅ G ₅ ggc cUGAuGagggccguuagggccGaa Acgguug B	15985	Hammerhead
175	C	GAGCGGU C ACAACCU	7232	19111	A ₅ G ₅ G ₅ U ₅ ugu cUGAuGagggccguuagggccGaa Accgcuc B	15986	Hammerhead
374	C	GUAAGGU C AUCGAUA	7233	19112	U ₅ A ₅ U ₅ C ₅ gau cUGAuGagggccguuagggccGaa Accuuac B	15987	Hammerhead
258	S27	UGGUGGUCCAUUAGCCCUAG	7234	22022	U ₅ G ₅ G ₅ U ₅ G ₅ G ₅ C ₅ U ₅ C ₅ A ₅ U ₅ C ₅ U ₅ A ₅ G ₅ C ₅ G ₅ U ₅ A ₅ G	15988	Antisense
259	S27	GGUGGUCCAUUAGCCCUAGU	7235	22023	G ₅ G ₅ U ₅ G ₅ G ₅ C ₅ U ₅ C ₅ A ₅ U ₅ C ₅ U ₅ A ₅ G ₅ C ₅ C ₅ U ₅ A ₅ G ₅ U	15989	Antisense
260	S27	GUGGUCCAUUAGCCCUAGUC	7236	22024	G ₅ U ₅ G ₅ G ₅ C ₅ U ₅ C ₅ A ₅ U ₅ C ₅ A ₅ U ₅ A ₅ G ₅ C ₅ C ₅ U ₅ A ₅ G ₅ U ₅ C	15990	Antisense
261	S27	UGGCUCCAUUAGCCCUAGUCA	7237	22025	U ₅ G ₅ G ₅ C ₅ U ₅ C ₅ A ₅ U ₅ C ₅ A ₅ U ₅ A ₅ G ₅ C ₅ C ₅ U ₅ A ₅ G ₅ U ₅ C ₅ A	15991	Antisense
262	S27	GGCUCCAUUAGCCCUAGUCAC	7238	22026	G ₅ G ₅ C ₅ U ₅ C ₅ A ₅ U ₅ C ₅ U ₅ A ₅ G ₅ C ₅ C ₅ U ₅ A ₅ G ₅ U ₅ C ₅ A ₅ C	15992	Antisense
263	S27	GCUCUCCAUUAGCCCUAGUCACG	7239	22027	G ₅ C ₅ U ₅ C ₅ A ₅ U ₅ C ₅ U ₅ A ₅ G ₅ C ₅ C ₅ U ₅ A ₅ G ₅ U ₅ C ₅ A ₅ C ₅ G	15993	Antisense
264	S27	CUCCAUUAGCCCUAGUCACGG	7240	22028	C ₅ U ₅ C ₅ A ₅ U ₅ C ₅ U ₅ A ₅ G ₅ C ₅ C ₅ U ₅ A ₅ G ₅ U ₅ C ₅ A ₅ C ₅ G ₅ G	15994	Antisense
265	S27	UCCAUUAGCCCUAGUCACGGC	7241	22029	U ₅ C ₅ C ₅ A ₅ U ₅ U ₅ A ₅ G ₅ C ₅ C ₅ U ₅ A ₅ G ₅ U ₅ C ₅ A ₅ C ₅ G ₅ G ₅ C	15995	Antisense
266	S27	CCAUCUAGCCCUAGUCACGGCU	7242	22030	C ₅ C ₅ A ₅ U ₅ C ₅ U ₅ A ₅ G ₅ C ₅ C ₅ U ₅ A ₅ G ₅ U ₅ C ₅ A ₅ C ₅ G ₅ G ₅ C ₅ U	15996	Antisense

139	HCV+	GAGAGCCAUAGUG	7278	22526	C ₅ A ₅ C ₅ U ₅ AU	CUGAUAGagggccguuagggccGaa	Icucuc B	16032	Inozyme
140	HCV+	AGAGCCAUAGUGG	7279	22527	C ₅ C ₅ A ₅ C ₅ UA	CUGAUAGagggccguuagggccGaa	Igcucu B	16033	Inozyme
281	HCV+	AAGGCCUUGUGGU	7280	22528	A ₅ C ₅ C ₅ A ₅ CA	CUGAUAGagggccguuagggccGaa	Igccuu B	16034	Inozyme
130	HCV+	CCUCCCCGGGAGA	7281	22529	U ₅ C ₅ U ₅ C ₅ CC	CUGAUAGagggccguuagggccGaa	Igaggg B	16035	Inozyme
280	HCV+	AAAGGCCUUGUGG	7282	22530	C ₅ C ₅ A ₅ C ₅ AA	CUGAUAGagggccguuagggccGaa	Iccuuu B	16036	Inozyme
149	HCV+	GUGGUCUCGCGGAA	7283	22531	U ₅ U ₅ C ₅ C ₅ GC	CUGAUAGagggccguuagggccGaa	Iaccac B	16037	Inozyme
194	HCV+	GGGUCCUUCUUG	7284	22532	C ₅ A ₅ A ₅ C ₅ AA	CUGAUAGagggccguuagggccGaa	Igaccc B	16038	Inozyme
255	HCV+	GUAGCCGAGUAG	7285	22533	C ₅ U ₅ A ₅ C ₅ UC	CUGAUAGagggccguuagggccGaa	Icuagc B	16039	Inozyme
294	HCV+	ACUGCCUGAUAGG	7286	22534	C ₅ C ₅ U ₅ A ₅ UC	CUGAUAGagggccguuagggccGaa	Igcagu B	16040	Inozyme
293	HCV+	UACUGCCUGAUAG	7287	22535	C ₅ U ₅ A ₅ U ₅ CA	CUGAUAGagggccguuagggccGaa	Icagua B	16041	Inozyme
290	HCV+	UGGUACUGCCUGA	7288	22536	U ₅ C ₅ A ₅ C ₅ GC	CUGAUAGagggccguuagggccGaa	Iuacca B	16042	Inozyme
169	HCV+	GUACACCGGAUU	7289	22537	A ₅ A ₅ U ₅ U ₅ CC	CUGAUAGagggccguuagggccGaa	Iuguac B	16043	Inozyme
293	HCV+	GUACUGCCUGAUAGG	7290	22544	C ₅ C ₅ U ₅ A ₅ UCA	CUGAUAGagggccguuagggccGaa	Icaguac B	16044	Inozyme
294	HCV+	UACUGCCUGAUAGG	7291	22545	C ₅ C ₅ C ₅ U ₅ AUC	CUGAUAGagggccguuagggccGaa	Igcagua B	16045	Inozyme
281	HCV+	AAAGGCCUUGUGGUA	7292	22546	U ₅ A ₅ C ₅ C ₅ A ₅ CA	CUGAUAGagggccguuagggccGaa	Igccuuu B	16046	Inozyme
166	HCV+	UGAGUACACCGGA	7293	22549	U ₅ C ₅ C ₅ A ₅ SGU	CUGAUAGagggccguuagggccGaa	Uacuca B	16047	Amberzyme
168	HCV+	AGUACACCGGAU	7294	22550	A ₅ U ₅ U ₅ C ₅ CG	CUGAUAGagggccguuagggccGaa	Uguacu B	16048	Amberzyme
141	HCV+	GAGCCAUAGUGGU	7295	22551	A ₅ C ₅ C ₅ A ₅ CU	CUGAUAGagggccguuagggccGaa	Uggcuc B	16049	Amberzyme
156	HCV+	GCGGAACCGGUGA	7296	22552	U ₅ C ₅ A ₅ C ₅ CG	CUGAUAGagggccguuagggccGaa	Uuccgc B	16050	Amberzyme
155	HCV+	UGCAGAACCGGUG	7297	22553	C ₅ A ₅ C ₅ C ₅ GG	CUGAUAGagggccguuagggccGaa	Uccgca B	16051	Amberzyme
289	HCV+	GUGGUACUGCCUG	7298	22554	C ₅ A ₅ SG ₅ CA	CUGAUAGagggccguuagggccGaa	Uaccac B	16052	Amberzyme
297	HCV+	GCCUGAUAGGGUG	7299	22555	C ₅ A ₅ C ₅ C ₅ CU	CUGAUAGagggccguuagggccGaa	Ucaggc B	16053	Amberzyme
166	HCV+	GUGAGUACACCGGAA	7300	22556	U ₅ U ₅ C ₅ C ₅ SGU	CUGAUAGagggccguuagggccGaa	Uacucac B	16054	Amberzyme
141	HCV+	AGAGCCAUAGUGGUC	7301	22557	SG ₅ A ₅ C ₅ CAU	CUGAUAGagggccguuagggccGaa	Uggcucu B	16055	Amberzyme
156	HCV+	UGCAGAACCGGUGAG	7302	22558	C ₅ U ₅ C ₅ A ₅ CCG	CUGAUAGagggccguuagggccGaa	Uuccgca B	16056	Amberzyme
155	HCV+	CUGCGGAACCGGUGA	7303	22559	U ₅ C ₅ A ₅ C ₅ CGG	CUGAUAGagggccguuagggccGaa	Uccgcag B	16057	Amberzyme
289	HCV+	UGUGGUACUGCCUGA	7304	22560	U ₅ C ₅ A ₅ SG ₅ CA	CUGAUAGagggccguuagggccGaa	Uaccaca B	16058	Amberzyme
297	HCV+	UGCUGAUAGGGUGC	7305	22561	SG ₅ C ₅ A ₅ C ₅ CCU	CUGAUAGagggccguuagggccGaa	Ucaggca B	16059	Amberzyme
168	HCV+	GAGUACACCGGAUU	7306	22562	A ₅ A ₅ U ₅ U ₅ CCG	CUGAUAGagggccguuagggccGaa	Uguacuc B	16060	Amberzyme
166	HCV-	UCCGGUGUACUCA	7307	22563	U ₅ SG ₅ A ₅ SG ₅ UA	gccgaaaagcGagugaGguCu	accgga B	16061	Zinzyme
168	HCV-	AUUCGGGUGUACU	7308	22564	A ₅ SG ₅ U ₅ A ₅ CA	gccgaaaagcGagugaGguCu	cggaaau B	16062	Zinzyme
138	HCV-	ACUAUGGCUCUCC	7309	22565	GG ₅ SG ₅ A ₅ SG ₅ AG	gccgaaaagcGagugaGguCu	cauagu B	16063	Zinzyme
156	HCV-	UCACCGGUUCCGC	7310	22566	GG ₅ C ₅ SG ₅ AA	gccgaaaagcGagugaGguCu	cgguga B	16064	Zinzyme
236	HCV-	GCGGGGCACGCC	7311	22567	GG ₅ SG ₅ C ₅ SG ₅ UG	gccgaaaagcGagugaGguCu	ccccgc B	16065	Zinzyme
279	HCV-	CACAAAGGCCUUUC	7312	22568	GG ₅ A ₅ SG ₅ A ₅ SGG	gccgaaaagcGagugaGguCu	cuugug B	16066	Zinzyme

151	HCV-	GGUCCGCAGACC	7313	22569	g ₉ s ₉ u ₉ c ₉ ug gccgaaaggCgagugaGguGcu ggaacc B	16067	Zinzyme
292	HCV-	UAUCAGGCAGUAC	7314	22570	g ₉ u ₉ a ₉ c ₉ ug gccgaaaggCgagugaGguGcu cugaua B	16068	Zinzyme
289	HCV-	CAGGCAGUACCAC	7315	22571	g ₉ u ₉ g ₉ g ₉ ua gccgaaaggCgagugaGguGcu ugccug B	16069	Zinzyme
166	HCV-	UUCGGUGUACUCAC	7316	22572	g ₉ u ₉ g ₉ a ₉ s ₉ ua gccgaaaggCgagugaGguGcu accggaa B	16070	Zinzyme
279	HCV-	CCACAAGGCCUUUCG	7317	22573	c ₉ g ₉ a ₉ a ₉ agg gccgaaaggCgagugaGguGcu cuugugg B	16071	Zinzyme
156	HCV-	CUCACCGGUUCCGCA	7318	22574	u ₉ g ₉ c ₉ g ₉ gaa gccgaaaggCgagugaGguGcu cggugag B	16072	Zinzyme
138	HCV-	CACUAUGGCUCUCCC	7319	22575	g ₉ g ₉ a ₉ s ₉ gag gccgaaaggCgagugaGguGcu cauagug B	16073	Zinzyme
151	HCV-	CGGUUCCGCAGACCA	7320	22576	u ₉ g ₉ s ₉ u ₉ cug gccgaaaggCgagugaGguGcu ggaaccg B	16074	Zinzyme
292	HCV-	CUAUCAGGCAGUACC	7321	22577	g ₉ g ₉ u ₉ a ₉ cug gccgaaaggCgagugaGguGcu cugauag B	16075	Zinzyme
289	HCV-	UCAGGCAGUACCACA	7322	22578	u ₉ g ₉ u ₉ g ₉ ua gccgaaaggCgagugaGguGcu ugccuga B	16076	Zinzyme
168	HCV-	AAUUCGGUGUACUC	7323	22579	g ₉ a ₉ g ₉ u ₉ aca gccgaaaggCgagugaGguGcu cggaaau B	16077	Zinzyme
163	HCV-	GGUGUACUACCG	7324	22580	c ₉ g ₉ g ₉ u ₉ sga cUGAUGaggccguuaggccGaa Uacacc B	16078	Amberzyme
159	HCV-	UACUCACCGGUUC	7325	22581	g ₉ a ₉ a ₉ c ₉ cg cUGAUGaggccguuaggccGaa Uagaua B	16079	Amberzyme
140	HCV-	CCACUAUAGGCUCU	7326	22582	a ₉ g ₉ a ₉ g ₉ cc cUGAUGaggccguuaggccGaa Uagugg B	16080	Amberzyme
281	HCV-	ACCACAAGGCCUU	7327	22583	a ₉ a ₉ g ₉ g ₉ cc cUGAUGaggccguuaggccGaa Uguugu B	16081	Amberzyme
233	HCV-	GGGGCACGCCCAA	7328	22584	u ₉ u ₉ g ₉ g ₉ gc cUGAUGaggccguuaggccGaa Ugcccc B	16082	Amberzyme
143	HCV-	AGACCACUAUGGC	7329	22585	g ₉ c ₉ c ₉ a ₉ ua cUGAUGaggccguuaggccGaa Uggucu B	16083	Amberzyme
146	HCV-	CGCAGACCACUAU	7330	22586	a ₉ u ₉ a ₉ g ₉ ug cUGAUGaggccguuaggccGaa Ucugcg B	16084	Amberzyme
195	HCV-	CCAAGAAAGGACC	7331	22587	g ₉ g ₉ u ₉ c ₉ cu cUGAUGaggccguuaggccGaa Ucuugg B	16085	Amberzyme
194	HCV-	CAAGAAAGGACCC	7332	22588	g ₉ g ₉ g ₉ u ₉ cc cUGAUGaggccguuaggccGaa Uucuug B	16086	Amberzyme
283	HCV-	GUACCACAAGGCC	7333	22589	g ₉ g ₉ c ₉ c ₉ uu cUGAUGaggccguuaggccGaa Ugguaa B	16087	Amberzyme
286	HCV-	GCAGUACCACAAG	7334	22590	c ₉ u ₉ u ₉ g ₉ ug cUGAUGaggccguuaggccGaa Uacugc B	16088	Amberzyme
296	HCV-	ACCCUAUCAGGCA	7335	22591	u ₉ g ₉ c ₉ s ₉ ug cUGAUGaggccguuaggccGaa Uagggg B	16089	Amberzyme
190	HCV-	AAAGGACCCGGUC	7336	22592	g ₉ a ₉ c ₉ s ₉ gg cUGAUGaggccguuaggccGaa Uccuuu B	16090	Amberzyme
163	HCV-	CGGUGUACUCACCGG	7337	22593	c ₉ c ₉ g ₉ g ₉ uga cUGAUGaggccguuaggccGaa Uacaccg B	16091	Amberzyme
140	HCV-	ACCACUAUGGCUCUC	7338	22594	g ₉ a ₉ g ₉ a ₉ g ₉ cc cUGAUGaggccguuaggccGaa Uaguggu B	16092	Amberzyme
159	HCV-	GUACUCACCGGUUCC	7339	22595	g ₉ g ₉ a ₉ s ₉ ccg cUGAUGaggccguuaggccGaa Uaguuac B	16093	Amberzyme
233	HCV-	GGGGGCACGCCCAAA	7340	22596	u ₉ u ₉ u ₉ g ₉ ggc cUGAUGaggccguuaggccGaa Ugcccc B	16094	Amberzyme
143	HCV-	CAGACCACUAUGGCU	7341	22597	a ₉ g ₉ c ₉ s ₉ ua cUGAUGaggccguuaggccGaa Uggucug B	16095	Amberzyme
146	HCV-	CCGCAGACCACUAUG	7342	22598	c ₉ a ₉ u ₉ s ₉ gug cUGAUGaggccguuaggccGaa Ucugcgg B	16096	Amberzyme
195	HCV-	UCCAAGAAAGGACCC	7343	22599	g ₉ g ₉ g ₉ u ₉ ccu cUGAUGaggccguuaggccGaa Ucuugga B	16097	Amberzyme
283	HCV-	AGUACCACAAGGCCU	7344	22600	a ₉ g ₉ g ₉ c ₉ uu cUGAUGaggccguuaggccGaa Ugguaa B	16098	Amberzyme
281	HCV-	UACCACAAGGCCUUU	7345	22601	a ₉ a ₉ g ₉ g ₉ g ₉ cc cUGAUGaggccguuaggccGaa Uguggua B	16099	Amberzyme
296	HCV-	CACCCUAUCAGGCAG	7346	22602	c ₉ u ₉ g ₉ s ₉ c ₉ ug cUGAUGaggccguuaggccGaa Uagggug B	16100	Amberzyme
286	HCV-	GGCAGUACCACAAGG	7347	22603	c ₉ c ₉ u ₉ u ₉ gug cUGAUGaggccguuaggccGaa Uacugcc B	16101	Amberzyme

7985	HCV-	UCUCAGU G UCUUCCA	7348	22719	uggaaga uGAUg gcaUGacuaugc gCg acugaga B	16102	G-cleaver
4832	HCV-	UGUAUAU G CCUCUCC	7349	22720	ggagagg uGAUg gcaUGacuaugc gCg auuaca B	16103	G-cleaver
4153	HCV-	ACCGUGU G CCUUAAGA	7350	22721	ucuaagg uGAUg gcaUGacuaugc gCg acacggg B	16104	G-cleaver
3200	HCV-	GUGGAGU G AGGUGGU	7351	22722	accaccu uGAUg gcaUGacuaugc gCg acuccac B	16105	G-cleaver
1682	HCV-	ACGAGUU G AACCCUGU	7352	22723	acagguu uGAUg gcaUGacuaugc gCg aacucgu B	16106	G-cleaver
896	HCV+	CCUGUCU G ACCAUCC	7353	22724	ggauggu uGAUg gcaUGacuaugc gCg agacagg B	16107	G-cleaver
2504	HCV+	UCCUGUU G CUUUUCC	7354	22725	ggaaaaa uGAUg gcaUGacuaugc gCg aacagga B	16108	G-cleaver
2651	HCV+	UCCUCGU G UUCUUCU	7355	22726	ggaagaa uGAUg gcaUGacuaugc gCg acgagga B	16109	G-cleaver
4094	HCV+	ACAAAGU G CUCGUCC	7356	22727	ggacgag uGAUg gcaUGacuaugc gCg acuuugu B	16110	G-cleaver
8970	HCV+	GCCACUU G ACCUACC	7357	22728	gguaggu uGAUg gcaUGacuaugc gCg aaguggc B	16111	G-cleaver
1200	HCV+	CUUCCUC G UCUCUCA	7358	22747	uagaga gccgaaaggcgagugagGuCu gaggaag B	16112	Zinzyne
1211	HCV+	CUCAGCU G UUCACCU	7359	22748	aggugaa gccgaaaggcgagugagGuCu agcugag B	16113	Zinzyne
2504	HCV+	UCCUGUU G CUUUUCC	7354	22749	ggaaaag gccgaaaggcgagugagGuCu aacagga B	16114	Zinzyne
2651	HCV+	UCCUGU G UUCUUCU	7355	22750	agaagaa gccgaaaggcgagugagGuCu acgagga B	16115	Zinzyne
8811	HCV+	CACUCCA G UCAACUC	7360	22751	gaguuga gccgaaaggcgagugagGuCu uggagug B	16116	Zinzyne
8594	HCV-	UCGCGCG G UCCUUCU	7361	22752	aagagga gccgaaaggcgagugagGuCu gcggcga B	16117	Zinzyne
7985	HCV-	UCUCAGU G UCUCUCA	7348	22753	uggaaga gccgaaaggcgagugagGuCu acugaga B	16118	Zinzyne
6611	HCV-	CCUCCAC G UACUCCU	7362	22754	aggagua gccgaaaggcgagugagGuCu guggagg B	16119	Zinzyne
5633	HCV-	UCCACAU G UGUUUGG	7363	22755	cgaagca gccgaaaggcgagugagGuCu augugga B	16120	Zinzyne
821	HCV-	UCACGCC G UCUCUCA	7364	22756	uggaaga gccgaaaggcgagugagGuCu ggcguga B	16121	Zinzyne
870	HCV+	CUCUAUC U UCCUUCU	7365	22775	aagagga CUGAUGAggcccguuaggccGAA Iauagag B	16122	Inozyme
1210	HCV+	UCUCAGC U GUTACAC	7366	22776	ggugaac CUGAUGAggcccguuaggccGAA Icuagga B	16123	Inozyme
2642	HCV+	UCCUCUC C UUCCUCG	7367	22777	cgaggaa CUGAUGAggcccguuaggccGAA Iagagga B	16124	Inozyme
5726	HCV+	UCACAGC C UCCUCCA	7368	22778	ugaugga CUGAUGAggcccguuaggccGAA Icuogga B	16125	Inozyme
8142	HCV+	CUCCACC C UUCUCCA	7369	22779	ugagga CUGAUGAggcccguuaggccGAA Iguggag B	16126	Inozyme
7990	HCV-	UGGUGUC U CAGUGUC	7370	22780	gacacug CUGAUGAggcccguuaggccGAA Iacacca B	16127	Inozyme
7813	HCV-	CUUCGCC U UCAUCUC	7371	22781	gagauga CUGAUGAggcccguuaggccGAA Igcgaaag B	16128	Inozyme
7137	HCV-	ACCUCUC U CUCAUCC	7372	22782	ggaugag CUGAUGAggcccguuaggccGAA Iagaggu B	16129	Inozyme
6084	HCV-	UUCAUCC A CUGCACA	7373	22783	ugugcag CUGAUGAggcccguuaggccGAA Igaugaa B	16130	Inozyme
2554	HCV-	CAACAGC A UCAUCCA	7374	22784	uggauga CUGAUGAggcccguuaggccGAA Icuugug B	16131	Inozyme
1202	HCV+	UCCUGU C UCUCAGC	7375	22943	gcugaga CUGAUGAggcccguuaggccGAA Acgagga B	16132	Hammerhead
1607	HCV+	GGCACAU U AACAGGA	7376	22944	uccuguu CUGAUGAggcccguuaggccGAA Augugcc B	16133	Hammerhead
2639	HCV+	GCAUCCU C UCCUUCU	7377	22945	ggaagga CUGAUGAggcccguuaggccGAA Aggaugc B	16134	Hammerhead
6610	HCV+	GAGGAGU A CGUGGAG	7378	22946	cuccacg CUGAUGAggcccguuaggccGAA Acuccuc B	16135	Hammerhead
9014	HCV+	GCGCAUU U UCACUCC	7379	22947	ggaguga CUGAUGAggcccguuaggccGAA Aaugcgc B	16136	Hammerhead
8605	HCV-	GACUCGU A GGCUCGC	7380	22948	gcgagcc CUGAUGAggcccguuaggccGAA Acgaguc B	16137	Hammerhead
7983	HCV-	UCAGUGU C UUCACGC	7381	22949	gcuggaa CUGAUGAggcccguuaggccGAA Acacuga B	16138	Hammerhead
7136	HCV-	CCUCUCU C UCAUCCU	7382	22950	aggauga CUGAUGAggcccguuaggccGAA Agagagg B	16139	Hammerhead
6609	HCV-	UCCACGU A CUCCUCA	7383	22951	ugaggag CUGAUGAggcccguuaggccGAA Acgugga B	16140	Hammerhead
6292	HCV-	CGUGCAU A UCCAGUC	7384	22952	gacugga CUGAUGAggcccguuaggccGAA Augcacg B	16141	Hammerhead
867	HCV+	UUUCUCU A UCUCUCC	7385	22971	aggaaaga GGCTAGCTACAACGA agagaaa B	16142	DNAzyme
1200	HCV+	CUUCCUC G UCUCUCA	7358	22972	uagaga GGCTAGCTACAACGA gaggaag B	16143	DNAzyme
1211	HCV+	CUCAGCU G UUCACCU	7359	22973	aggugaa GGCTAGCTACAACGA agcugag B	16144	DNAzyme
5730	HCV+	AGCCUCC A UCACCAG	7386	22974	cugguga GGCTAGCTACAACGA ggaggcu B	16145	DNAzyme
6533	HCV+	UCAACGC A UACACCA	7387	22975	uggugua GGCTAGCTACAACGA gcuugua B	16146	DNAzyme

8594	HCV-	UCGCCGC G UCCUCUU	7361	22976	aagagga GGCTAGCTACAACGA gcggcga B	16147	DNAzyme
7810	HCV-	CGCCUUC A UCUCUU	7388	22977	aaggaga GGCTAGCTACAACGA gaaggcg B	16148	DNAzyme
7133	HCV-	CUCUCUC A UCCUCCU	7389	22978	aggagga GGCTAGCTACAACGA gagagag B	16149	DNAzyme
6611	HCV-	CCUCCAC G UACUCCU	7362	22979	aggagua GGCTAGCTACAACGA guggagg B	16150	DNAzyme
2300	HCV-	CCUCCAA A UCACAAAC	7390	22980	guuguga GGCTAGCTACAACGA uuggagg B	16151	DNAzyme
195	HCV+	GGGUCCU U UCUUGGA	7148	23072	c _S c _S a _S a _S ga cUGAuGaggcgWWagccGaa Aggacc B	16152	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	23076	WWWWC _S C _S a _S a _S ga cUGAuGaggcguuagccGaa Aggacc B	16153	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	23077	WWWC _S C _S a _S a _S ga cUGAuGaggcgWWWagccGaa Aggacc B	16154	Hammerhead
195	HCV+	GGGUCCU U UCUUGGA	7148	23086	c _S c _S a _S a _S ga cUGAuGaggcgWWWagccGaa Aggacc B	16155	Hammerhead

lower case = 2'-O-methyl
UPPER CASE = RIBO
B = inverted deoxy abasic
U = 2'-deoxy-2'-amino Uridine
C = 2'-deoxy-2'-amino Cytidine
U = 2'-deoxy-2'-amino Uridine
Z = BRdU (5-bromo-2'-deoxy Uridine)
W = **acyclic galactose-amine linker**

UNDERLINE = deoxy nucleotide

TABLE XXI: ANTI HCV AMINO CONTAINING HAMMERHEAD RIBOZYME AND CONTROL SEQUENCES

pos	RPI#	HCV 5'UTR Site	Ribozyme Sequences (5'-3')		Core	Rz Seq ID
62	12257	HCV-62	g _s c _s g _s ugaa	cUGAUGaggccguuaggccGaa	AcaguagB	Active 15897
79	12258	HCV-79	a _s u _s g _s gcua	cUGAUGaggccguuaggccGaa	AcgcuuuB	Active 15898
81	12249	HCV-81	c _s c _s a _s uggc	cUGAUGaggccguuaggccGaa	AgacgcuB	Active 15899
104	12259	HCV-104	g _s c _s u _s gcac	cUGAUGaggccguuaggccGaa	AcacucaB	Active 15900
142	12250	HCV-142	a _s g _s a _s ccac	cUGAUGaggccguuaggccGaa	AuggcucB	Active 15901
148	12251	HCV-148	u _s u _s c _s cgca	cUGAUGaggccguuaggccGaa	AccacuaB	Active 15902
165	12260	HCV-165	u _s c _s c _s ggug	cUGAUGaggccguuaggccGaa	AcucaccB	Active 15903
192	12261	HCV-192	a _s a _s g _s aaag	cUGAUGaggccguuaggccGaa	AcccgguB	Active 15904
195	12252	HCV-195	u _s c _s c _s aaga	cUGAUGaggccguuaggccGaa	AggaccCB	Active 15905
196	12262	HCV-196	a _s u _s c _s caag	cUGAUGaggccguuaggccGaa	AaggaccB	Active 15906
270	12263	HCV-270	c _s u _s u _s ucgc	cUGAUGaggccguuaggccGaa	AcccaacB	Active 15907
282	12264	HCV-282	g _s u _s a _s ccac	cUGAUGaggccguuaggccGaa	AggccuuB	Active 15908
306	12265	HCV-306	c _s a _s c _s ucgc	cUGAUGaggccguuaggccGaa	AgcaccCB	Active 15909
325	12253	HCV-325	u _s c _s u _s acga	cUGAUGaggccguuaggccGaa	AccuccCB	Active 15910
330	12254	HCV-330	c _s a _s c _s gguc	cUGAUGaggccguuaggccGaa	AcgagacB	Active 15911
Control Sequences						
79	13274	HCV-79 AC2	c _s u _s u _s aggu	cUAGUGaggccguuaggccGau	AguucucB	Attenuated 16171
81	13271	HCV-81 AC	u _s c _s u _s gccg	cUAGUGaggccguuaggccGau	AgugaccB	Attenuated 16172
142	13270	HCV-142 AC	a _s a _s c _s ccug	cUAGUGaggccguuaggccGau	AgcucguB	Attenuated 16173
192	13272	HCV-192 AC	a _s g _s u _s agaa	cUAGUGaggccguuaggccGau	AgcugccB	Attenuated 16174
195	13269	HCV-195 AC	g _s a _s u _s ucca	cUAGUGaggccguuaggccGau	AcgcgacB	Attenuated 16175
282	13273	HCV-282 AC	g _s c _s c _s auuc	cUAGUGaggccguuaggccGau	AucuggcB	Attenuated 16176
330	13268	HCV-330 AC	c _s c _s a _s ggcu	cUAGUGaggccguuaggccGau	AaugcgcB	Attenuated 16177
195	15291	HCV-195 BAC3	u _s c _s c _s aaga	cUAGUGacgccguuaggcgGaa	AggaccCB	Attenuated 16178
195	15292	HCV-195 SAC3	a _s g _s a _s cuac	cUAGUGacgccguuaggcgGaa	AcccgagB	Attenuated 16179
330	15294	HCV-330 BAC	c _s a _s c _s gguc	cUAGUGacgccguuaggcgGaa	AcgagacB	Attenuated 16180
330	15295	HCV-330 SAC	g _s c _s u _s ccga	cUAGUGacgccguuaggcgGaa	AgacacgB	Attenuated 16181

UPPER CASE = RIBO; lower case = 2'-O-methyl; B = inverted deoxyabasic;

s = phosphorothioate linkage

U = 2'-deoxy-2'-amino uridine

**TABLE XXII: ANTI HCV SITE 330 ANTISENSE NUCLEIC ACID AND
SCRAMBLED CONTROL SEQUENCES**

pos	RPI #	Alias	Antisense Nucleic Acid	Seq ID #
330	17501	HCV.5-330 antisense	G _s T _s G _s C _s T _s C _s A _s T _s G _s A _s T _s G _s C _s A _s C _s G _s G _s T _s C _s T	15898
330	17498	HCV.5-330 antisense	G _s T _s G _s C _s T _s C _s A _s T _s G _s G _s T _s G _s C _s A _s C _s G _s G _s T _s C _s T	16182

pos	RPI#	Alias	Control Sequence	Seq ID #
330	17499	HCV.5-330 scrambled	T _s G _s A _s T _s C _s A _s G _s G _s T _s C _s T _s G _s C _s T _s G _s C _s G _s T _s G _s C	16183
330	17502	HCV.5-330 Scrambled	T _s G _s A _s T _s C _s A _s G _s G _s T _s C _s T _s G _s C _s T _s G _s C _s A _s T _s G _s C	16184

UPPER CASE = Deoxy Nucleotide
s = phosphorothioate

TABLE XXIII: IN VITRO CLEAVAGE DATA, ANTI-HCV ENZYMATIC NUCLEIC ACIDS

Seq ID #	RPI#	Motif	Site (+/-)	Enzymatic Nucleic Acid Sequence	% Substrate Cleaved in 3 hours	Substrate Sequence	Seq ID #	Substrate RPI#
16132	22943	Hammerhead	1190 (+)	gcugaga CUGAUGAggcccguuaggccGAA Acgagga B	89.67	UCCUCGU C UCUCAGC B	7391	22897
16133	22944	Hammerhead	1595 (+)	uccuguu CUGAUGAggcccguuaggccGAA Augugcc B	90.33	GGCACAU U AACAGGA B	7392	22898
16134	22945	Hammerhead	2627 (+)	ggaagga CUGAUGAggcccguuaggccGAA Aggaugc B	82.54	GGAUCCU C UCCUCC B	7393	22899
16135	22946	Hammerhead	6598 (+)	cuccacg CUGAUGAggcccguuaggccGAA Acuccuc B	78.06	GAGGAGU A CGUGGAG B	7394	22900
16136	22947	Hammerhead	9002 (+)	ggaguga CUGAUGAggcccguuaggccGAA Aaugcgc B	81.88	GCGCAUU U UCACUCC B	7395	22901
16137	22948	Hammerhead	818 (-)	gcgagcc CUGAUGAggcccguuaggccGAA Acgaguc B	88.34	GACUCGU A GGCUCGC B	7396	22902
16138	22949	Hammerhead	1440 (-)	gcuggaa CUGAUGAggcccguuaggccGAA Acacuga B	89.16	UCAGUGU C UUCCAGC B	7397	22903
16139	22950	Hammerhead	2287 (-)	aggauga CUGAUGAggcccguuaggccGAA Agagagg B	83.43	CCUCUCU C UCAUCCU B	7398	22904
16140	22951	Hammerhead	2814 (-)	ugaagag CUGAUGAggcccguuaggccGAA Acguuga B	83.25	UCCACGU A CUCCUCA B	7399	22905
16141	22952	Hammerhead	3131 (-)	gacugga CUGAUGAggcccguuaggccGAA Augcacg B	86.96	CGUGCAU A UCCAGUC B	7400	22906
16142	22971	DNAzyme	855 (+)	aggaga GGC TAGCTACAACGA agagaaa B	92.11	UUUCUCU A UCUUCCU B	7401	22925
16143	22972	DNAzyme	1188 (+)	ugagaga GGC TAGCTACAACGA gaggaag B	86.38	CUUCCUC G UCUCUCA B	7402	22926
16144	22973	DNAzyme	1199 (+)	aggugaa GGC TAGCTACAACGA agcugag B	83.15	CUCAGCU G UUCACCU B	7403	22927
16145	22974	DNAzyme	5718 (+)	cugguga GGC TAGCTACAACGA ggaggcu B	57.82	AGCCUCC A UCACCA B	7404	22928
16146	22975	DNAzyme	6521 (+)	uggugua GGC TAGCTACAACGA gcuuga B	75.77	UCAACGC A UACACCA B	7405	22929
16147	22976	DNAzyme	829 (-)	aagagga GGC TAGCTACAACGA gcggcga B	66.06	UCGCCGC G UCCUCUU B	7406	22930
16148	22977	DNAzyme	1613 (-)	aaggaga GGC TAGCTACAACGA gaaggcg B	71.28	CGCCUUC A UCUCUUU B	7407	22931
16149	22978	DNAzyme	2290 (-)	aggagga GGC TAGCTACAACGA gagagag B	61.60	CUCUCUC A UCCUCCU B	7408	22932
16150	22979	DNAzyme	2812 (-)	aggagua GGC TAGCTACAACGA guggagg B	85.53	CCUCCAC G UACUCCU B	7409	22933
16151	22980	DNAzyme	7123 (-)	guuguga GGC TAGCTACAACGA uuggagg B	34.60	CCUCCAA A UCACAAC B	7410	22934
16102	22719	G-cleaver	1438 (+)	uggaaga uGALg gcauGcacuagc gCg acugaga B	69.88	UCUCAGU G UCUUCCA B	7411	22813
16103	22720	G-cleaver	4591 (+)	ggagagg uGALg gcauGcacuagc gCg auauaca B	77.74	UGUAUUAU G CCUCUCC B	7412	22814
16104	22721	G-cleaver	5270 (+)	ucuaagg uGALg gcauGcacuagc gCg acacggu B	47.37	ACCGUGU G CCUUAAG B	7413	22815
16105	22722	G-cleaver	6223 (+)	accaccu uGALg gcauGcacuagc gCg acuccac B	75.84	GUGGAGU G AGGUGGU B	7414	22816
16106	22723	G-cleaver	7741 (+)	acagguu uGALg gcauGcacuagc gCg aacucgu B	61.58	ACGAGUU G AACCUGU B	7415	22817
16107	22724	G-cleaver	884 (-)	ggauugu uGALg gcauGcacuagc gCg agacagg B	65.16	CCUGUCU G ACCAUCC B	7416	22818
16108	22725	G-cleaver	2492 (-)	ggaaaag uGALg gcauGcacuagc gCg aacagga B	94.66	UCCUGUU G CUUUUCC B	7417	22819
16109	22726	G-cleaver	2639 (-)	agaagaa uGALg gcauGcacuagc gCg acgagga B	82.14	UCCUCGU G UUCUUCU B	7418	22820

16110	22727	G-cleaver	4082 (-)	ggacgag uGAlg gcaUGcacuagc gCg acuuugu B	67.20	ACAAAGU G CUCGUCC B	7419	22821
16111	22728	G-cleaver	8958 (-)	gguaggu uGAlg gcaUGcacuagc gCg aaguggc B	81.06	GCCACUU G ACCUACC B	7420	22822

16112	22747	Zinzyme	1188 (+)	ugagaga gccgaaaggGgagugaGGuCu gaggaag B	66.11	CUUCCUC G UCUCUCA B	7402	22841
16113	22748	Zinzyme	1199 (+)	agguaga gccgaaaggGgagugaGGuCu agcugag B	80.28	CUCAGCU G UUCACCU B	7403	22842
16114	22749	Zinzyme	2492 (+)	ggaag gccgaaaggGgagugaGGuCu aacagga B	90.80	UCCUGUU G CUUUUCC B	7417	22843
16115	22750	Zinzyme	2639 (+)	agaagaa gccgaaaggGgagugaGGuCu acgagga B	80.64	UCCUCGU G UUCUUCU B	7418	22844
16116	22751	Zinzyme	8799 (+)	gaguaga gccgaaaggGgagugaGGuCu uggagug B	14.85	CACUCCA G UCAACUC B	7421	22845
16117	22752	Zinzyme	829 (-)	aagagga gccgaaaggGgagugaGGuCu gccgcca B	27.83	UCGCCGC G UCCUCUU B	7406	22846
16118	22753	Zinzyme	1438 (-)	uggaaga gccgaaaggGgagugaGGuCu acugaga B	89.39	UCUCAGU G UCUUCCA B	7411	22847
16119	22754	Zinzyme	2812 (-)	aggagua gccgaaaggGgagugaGGuCu guggagg B	50.40	CCUCCAC G UACUCCU B	7409	22848
16120	22755	Zinzyme	3790 (-)	cgaagca gccgaaaggGgagugaGGuCu augugga B	81.10	UCCACAU G UGUUUCG B	7422	22849
16121	22756	Zinzyme	8602 (-)	uggaaga gccgaaaggGgagugaGGuCu gccguga B	73.47	UCACGCC G UCUUCCA B	7423	22850

16122	22775	Inozyme	858 (+)	aagagga CUGAUGAggcccguuaggccGAA laugag B	87.74	CUCUAUC U UCCUCUU B	7424	22869
16123	22776	Inozyme	1198 (+)	ggugaac CUGAUGAggcccguuaggccGAA lcugaga B	84.55	UCUCAGC U GUUCACC B	7425	22870
16124	22777	Inozyme	2630 (+)	cgaggaa CUGAUGAggcccguuaggccGAA lagagga B	90.12	UCCUCUC C UUCGUCC B	7426	22871
16125	22778	Inozyme	5714 (+)	ugaugga CUGAUGAggcccguuaggccGAA lcuguga B	83.77	UCACAGC C UCCAUCA B	7427	22872
16126	22779	Inozyme	8130 (+)	ugaggaa CUGAUGAggcccguuaggccGAA lguggag B	82.22	CUCCACC C UUCUCCA B	7428	22873
16127	22780	Inozyme	1433 (-)	gacacug CUGAUGAggcccguuaggccGAA lacacca B	87.33	UGGUGUC U CAGUGUC B	7429	22874
16128	22781	Inozyme	1610 (-)	gagauga CUGAUGAggcccguuaggccGAA lgcgaag B	70.67	CUUCGCC U UCAUCUC B	7430	22875
16129	22782	Inozyme	2286 (-)	ggaugag CUGAUGAggcccguuaggccGAA lagaggu B	78.83	ACCUCUC U CUCAUCC B	7431	22876
16130	22783	Inozyme	3339 (-)	ugugcag CUGAUGAggcccguuaggccGAA lgaugaa B	86.93	UUCAUCC A CUGCACA B	7432	22877
16131	22784	Inozyme	6869 (-)	uggauga CUGAUGAggcccguuaggccGAA lcuguug B	90.41	CAACAGC A UCAUCCA B	7433	22878

In vitro cleavage in 50 mM Tris-Cl, pH 8.0, 40 mM Mg²⁺ at 37°, using trace substrate, and enzymatic nucleic acid concentration of 500 nM or greater.

UPPER CASE = RIBO

UNDERLINED = DEOXY

lower case = 2'-O-methyl

B = inverted deoxybasic

C = 2'-amino C

(+/-) = plus strand/minus strand of HCV genome